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(54) Title: SYNTHETIC PEPTIDES AND USES THEREFORE

(57) Abstract: A synthetic polypeptide is disclosed, which comprises a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide. Synthetic polynucleotides are also disclosed that code for the synthetic polypeptides of the invention as well as expression constructs comprising the synthetic polynucleotides. Also disclosed are methods for constructing the aforementioned molecules and immunopotentiating compositions and methods for treating and/or preventing a disease or condition.



#### SYNTHETIC PEPTIDES AND USES THEREFORE

#### FIELD OF THE INVENTION

THIS INVENTION relates generally to agents for modulating immune responses. More particularly, the present invention relates to a synthetic polypeptide comprising a plurality of different segments of a parent polypeptide, wherein the segments are linked to each other such that one or more functions of the parent polypeptide are impeded, abrogated or otherwise altered and such that the synthetic polypeptide, when introduced into a suitable host, can elicit an immune response against the parent polypeptide. The invention also relates to synthetic polynucleotides encoding the synthetic polypeptides and to synthetic constructs comprising these polynucleotides. The invention further relates to the use of the polypeptides and polynucleotides of the invention in compositions for modulating immune responses. The invention also extends to methods of using such compositions for prophylactic and/or therapeutic purposes.

Bibliographic details of various publications referred to in this specification are collected at the end of the description.

#### **BACKGROUND OF THE INVENTION**

The modern reductionist approach to vaccine and therapy development has been pursued for a number of decades and attempts to focus only on those parts of pathogens or of cancer proteins which are relevant to the immune system. To date the performance of this approach has been relatively poor considering the vigorous research carried out and the number of effective vaccines and therapies that it has produced. This approach is still being actively pursued, however, despite its poor performance because vaccines developed using this approach are often extremely safe and because only by completely understanding the immune system can new vaccine strategies be developed.

One area that has benefited greatly from research efforts is knowledge about how the adaptive immune system operates and more specifically how T and B cells learn to recognise specific parts of pathogens and cancers. T cells are mainly involved in cell-mediated immunity whereas B cells are involved in the generation of antibody-mediated immunity. The two most important types of T cells involved in adaptive cellular immunity

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are αβ CD8<sup>+</sup> cytotoxic T lymphocytes (CTL) and CD4<sup>+</sup> T helper lymphocytes. CTL are important mediators of cellular immunity against many viruses, tumours, some bacteria and some parasites because they are able to kill infected cells directly and secrete various factors which can have powerful effects on the spread of infectious organisms. CTLs recognise epitopes derived from foreign intracellular proteins, which are 8-10 amino acids long and which are presented by class I major histocompatibility complex (MHC) molecules (in humans called human lymphocyte antigens - HLAs) (Jardetzky et al., 1991; Fremont et al., 1992; Rotzschke et al., 1990). T helper cells enhance and regulate CTL responses and are necessary for the establishment of long-lived memory CTL. They also inhibit infectious organisms by secreting cytokines such as IFN-y. T helper cells recognise epitopes derived mostly from extracellular proteins which are 12-25 amino acids long and which are presented by class II MHC molecules (Chicz et al., 1993; Newcomb et al., 1993). B cells, or more specifically the antibodies they secrete, are important mediators in the control and clearance of mostly extracellular organisms. Antibodies recognise mainly conformational determinants on the surface of organisms, for example, although sometimes they may recognise short linear determinants.

Despite significant advances towards understanding how T and linear B cell epitopes are processed and presented to the immune system, the full potential of epitopebased vaccines has not been fully exploited. The main reason for this is the large number of different T cell epitopes, which have to be included into such vaccines to cover the extreme HLA polymorphism in the human population. The human HLA diversity is one of the main reasons why whole pathogen vaccines frequently provide better population coverage than subunit or peptide-based vaccine strategies. There is a range of epitopebased strategies though which have tried to solve this problem, e.g., peptide blends, peptide conjugates and polyepitope vaccines (ie comprising strings of multiple epitopes) (Dyall et al., 1995; Thomson et al., 1996; Thomson et al., 1998; Thomson et al., 1998). These approaches however will always be sub optimal not only because of the slow pace of epitope characterisation but also, because it is virtually impossible for them to cover every existing HLA polymorphism in the population. A number of strategies have sought to avoid both problems by not identifying epitopes and instead incorporating larger amounts of sequence information e.g., approaches using whole genes or proteins and approaches that mix multiple protein or gene sequences together. The proteins used by these strategies

however sometimes still function and therefore can compromise vaccine safety e.g., whole cancer proteins. Alternative strategies have tried to improve the safety of vaccines by fragmenting the genes and expressing them either separately or as complex mixtures e.g., library DNA immunisation or by ligating such fragments back together. These approaches are still sub-optimal because they are too complex, generate poor levels of immunity, cannot guarantee that all proteins no longer function and/or that all fragments are present, which compromises substantially complete immunological coverage.

The lack of a safe and efficient vaccine strategy that can provide substantially complete immunological coverage is an important problem, especially when trying to develop vaccines against rapidly mutating and persistent viruses such as HIV and hepatitis C virus, because partial population coverage could allow vaccine-resistant pathogens to reemerge in the future. Human immunodeficiency virus (HIV) is an RNA lentivirus virus approximately 9 kb in length, which infects CD4<sup>+</sup> T cells, causing T cell decline and AIDS typically 3-8 years after infection. It is currently the most serious human viral infection. evidenced by the number of people currently infected with HIV or who have died from AIDS, estimated by the World Health Organisation (WHO) and UNAIDS in their AIDS epidemic update (December 1999) to be 33.6 and 16.3 million people, respectively. The spread of HIV is also now increasing fastest in areas of the world where over half of the human population reside, hence an effective vaccine is desperately needed to curb the spread of this epidemic. Despite the urgency, an effective vaccine for HIV is still some way off because of delays in defining the correlates of immune protection, lack of a suitable animal model, existence of up to 8 different subtypes of HIV and a high HIV mutation rate.

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A significant amount of research has been carried out to try and develop a vaccine capable of generating neutralising antibody responses that can protect against field isolates of HIV. Despite these efforts, it is now clear that the variability, instability and inaccessibility of critical determinants on the HIV envelope protein will make it extremely difficult and perhaps impossible to develop such a vaccine (Kwong et al., 1998). The limited ability of antibodies to block HIV infection is also supported by the observation that development of AIDS correlates primarily with a reduction in CTL responsiveness to HIV and not to altered antibody levels (Ogg et al., 1998). Hence CTL-mediated and not antibody-mediated responses appear to be critical for maintaining the asymptomatic state

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in vivo. There is also some evidence to suggest that pre-existing HIV-specific CTL responses can block the establishment of a latent HIV infection. This evidence comes from a number of cases where individuals have generated HIV-specific CTL responses without becoming infected and appear to be protected from establishing latent HIV infections despite repeated virus exposure (Rowland-Jones et al., 1995; Parmiani 1998). Taken together, these observations suggest that a vaccine capable of generating a broad range of strong CTL responses may be able to stop individuals from becoming latently infected with HIV or at least allow infected individuals to remain asymptomatic for life. Virtually all of the candidate HIV vaccines developed to date have been derived from subtype B HIV proteins (western world subtype) whereas the majority of the HIV infections worldwide are caused by subtypes A/E or C (E and A are similar except in the envelop protein)(referred to as developing world subtypes). Hence existing candidate vaccines may not be suitable for the more common HIV subtypes. Recently, there has been some evidence that B subtype vaccines may be partially effective against other common HIV subtypes (Rowland-Jones et al., 1998). Accordingly, the desirability of a vaccine still remains, whose effectiveness is substantially complete against all isolates of all strains of HIV.

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#### SUMMARY OF THE INVENTION

The present invention is predicated in part on a novel strategy for enhancing the efficacy of an immunopotentiating composition. This strategy involves utilising the sequence information of a parent polypeptide to produce a synthetic polypeptide that comprises a plurality of different segments of the parent polypeptide, which are linked sequentially together in a different arrangement relative to that of the parent polypeptide. As a result of this change in relationship, the sequence of the linked segments in the synthetic polypeptide is different to a sequence contained within the parent polypeptide. As more fully described hereinafter, the present strategy is used advantageously to cause significant disruption to the structure and/or function of the parent polypeptide while minimising the destruction of potentially useful epitopes encoded by the parent polypeptide.

Thus, in one aspect of the present invention, there is provided a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide.

In one embodiment, the synthetic polypeptide consists essentially of different segments of a single parent polypeptide.

In an alternate embodiment, the synthetic polypeptide consists essentially of different segments of a plurality of different parent polypeptides.

Suitably, said segments in said synthetic polypeptide are linked sequentially in a different order or arrangement relative to that of corresponding segments in said at least one parent polypeptide.

Preferably, at least one of said segments comprises partial sequence identity or homology to one or more other said segments. The sequence identity or homology is preferably contained at one or both ends of said at least one segment.

In another aspect, the invention resides in a synthetic polynucleotide encoding the synthetic polypeptide as broadly described above.

According to yet another aspect, the invention contemplates a synthetic construct comprising a said polynucleotide as broadly described above that is operably linked to a regulatory polynucleotide.

In a further aspect of the invention, there is provided a method for producing a synthetic polynucleotide as broadly described above, comprising:

- linking together in the same reading frame a plurality of nucleic acid sequences encoding different segments of at least one parent polypeptide to form a synthetic polynucleotide whose sequence encodes said segments linked together in a different relationship relative to their linkage in the at least one parent polypeptide.

Preferably, the method further comprises fragmenting the sequence of a respective parent polypeptide into fragments and linking said fragments together in a different relationship relative to their linkage in said parent polypeptide sequence. In a preferred embodiment of this type, the fragments are randomly linked together.

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Suitably, the method further comprises reverse translating the sequence of a respective parent polypeptide or a segment thereof to provide a nucleic acid sequence encoding said parent polypeptide or said segment. In a preferred embodiment of this type, an amino acid of said parent polypeptide sequence is reverse translated to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest. Suitably, an amino acid of said parent polypeptide sequence is reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence (e.g., a palindromic sequence or a duplicated sequence) that is refractory to the execution of a task (e.g., cloning or sequencing).

In another aspect, the invention encompasses a computer program product for designing the sequence of a synthetic polypeptide as broadly described above, comprising:

- code that receives as input the sequence of at least one parent polypeptide;
- code that fragments the sequence of a respective parent polypeptide into fragments;

- code that links together said fragments in a different relationship relative to their linkage in said parent polypeptide sequence; and
  - a computer readable medium that stores the codes.

In yet another aspect, the invention provides a computer program product for designing the sequence of a synthetic polynucleotide as broadly described above, comprising:

- code that receives as input the sequence of at least one parent polypeptide;
- code that fragments the sequence of a respective parent polypeptide into fragments;
- code that reverse translates the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment;
  - code that links together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence; and
    - a computer readable medium that stores the codes.

In still yet another aspect, the invention provides a computer for designing the sequence of a synthetic polypeptide as broadly described above, wherein said computer comprises:

- 20 (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
  - (b) a working memory for storing instructions for processing said machine-readable data;
- (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polypeptide sequence; and
  - (d) an output hardware coupled to said central processing unit, for receiving said synthetic polypeptide sequence.

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In a preferred embodiment, the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments and linking together said fragments in a different relationship relative to their linkage in the sequence of said parent polypeptide.

In still yet another aspect, the invention resides in a computer for designing the sequence of a synthetic polynucleotide as broadly described above, wherein said computer comprises:

- (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
- (b) a working memory for storing instructions for processing said machine-readable data;
- (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polynucleotide sequence; and
- (d) an output hardware coupled to said central processing unit, for receiving said synthetic polynucleotide sequence.

In a preferred embodiment, the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments, reverse translating the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment and linking together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence.

According to another aspect, the invention contemplates a composition, comprising an immunopotentiating agent selected from the group consisting of a synthetic polypeptide as broadly described above, a synthetic polynucleotide as broadly described above and a synthetic construct as broadly described above, together with a pharmaceutically acceptable carrier.

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The composition may optionally comprise an adjuvant.

In a further aspect, the invention encompasses a method for modulating an immune response, which response is preferably directed against a pathogen or a cancer, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from the group consisting of a synthetic polypeptide as broadly described above, a synthetic polynucleotide as broadly described above and a synthetic construct as broadly described above, or a composition as broadly described above.

According to still a further aspect of the invention, there is provided a method for treatment and/or prophylaxis of a disease or condition, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from the group consisting of a synthetic polypeptide as broadly described above, a synthetic polynucleotide as broadly described above and a synthetic construct as broadly described above, or a composition as broadly described above.

The invention also encompasses the use of the synthetic polypeptide, the synthetic polynucleotide and the synthetic construct as broadly described above in the study, and modulation of immune responses.

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#### **BRIEF DESCRIPTION OF THE DRAWINGS**

Figure 1 is a diagrammatic representation showing the number of people living with AIDS in 1998 in various parts of the world and most prevalent HIV clades in these regions. Estimates generated by UNAIDS.

Figure 2 is a graphical representation showing trends in the incidence of the common HIV clades and estimates for the future. Graph from the International Aids Vaccine Initiative (IAVI).

Figure 3 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV gag [SEQ ID NO: 1] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV gag protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 4 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV pol [SEQ ID NO: 2] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV pol protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton 20 Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR98-485.

Figure 5 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV vif [SEQ ID NO: 3] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade 25 consensus sequences for the HIV vif protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR98-485.

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Figure 6 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV vpr [SEQ ID NO: 4] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV vpr protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 7 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV tat [SEQ ID NO: 5] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV tat protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

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Figure 8 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV rev [SEQ ID NO: 6] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV rev protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 9 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV vpu [SEQ ID NO: 7] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV vpu protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 10 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV env [SEQ ID NO: 8] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade

consensus sequences for the HIV env protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 11 is a diagrammatic representation showing overlapping segments of a parent polypeptide sequence for HIV nef [SEQ ID NO: 9] used for the construction of an embodiment of an HIV Savine. Also shown are the alignments of common HIV clade consensus sequences for the HIV nef protein from the HIV Molecular Immunology Database 1997, Editors Bette Korber, John Moore, Cristian Brander, Richard Koup, Barton 10 Haynes and Bruce Walker. Publisher, Los Alamos National Laboratory, Theoretical Biology and Biophysics, Los Alamos, New Mexico, Pub LAUR 98-485.

Figure 12 is a diagrammatic representation depicting the systematic segmentation of the designed degenerate consensus sequences for each HIV protein and the reverse translation of each segment into a DNA sequence. Also shown is the number of segments used during random rearrangement and amino acids that were removed. Amino acids surrounded by an open square were removed from the design, because degenerate codons to cater for the desired amino acid combination required too many degenerate bases to comply with the incorporation of degenerate sequence rules outlined in the description of the invention herein. Amino acids surrounded by an open circle were removed only in the segment concerned mainly because they were coded for in an oligonucleotide overlap region. Amino acids marked with an asterisk were designed differently in one fragment compared to the corresponding overlap region (see tat gene)

Figure 13 is a diagrammatic representation showing the first and second most frequently used codons in mammals used to reverse translate HIV protein segments. Also shown are all first and second most frequently used degenerate codons for two amino acids where only one base is varied. Codons used where more than one base was varied were worked out in each case by comparing all the codons for each amino acid. The IUPAC codes for degenerate bases are also shown.

Figure 14 illustrates the construction plan for the HIV Savine showing the approximate sizes of the subcassettes, cassettes and full-length Savine cDNA and the restriction sites involved in joining them together. Also shown are the extra sequences

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added onto each subcassette during their design and a brief description of how the subcassettes, cassettes and full length cDNA were constructed and transferred into appropriate DNA plasmids. Description of full length construction: pA was cleaved with Xhol/SalI and cloned into XhoI arms of the B cassette; pAB was cleaved with XhoI and 5 cloned into XhoI arms of the C cassette; full length construct is excisable with either Xbal/BamHI at the 5' end or BglII at the 3' end. Options for excising cassettes: A) Xbal/BamHI at the 5' end, Bg/II/XhoI at the 3' end; B) Xbal/BamHI at the 5' end, Bg/II/SalI at the 3' end; C) Xbal/BamHI at the 5' end, Bg/II/SalI at the 3' end. Cleaving plasmid vectors: pDNAVacc is cleavable with Xbal/XhoI (DNA vaccination); pBCB07 or 10 pTK7.5 vectors are cleavable with BamHI/SalI (Recombinant Vaccinia); pAvipox vector pAF09 is cleavable with BamHI/SalI (Recombinant Avipox).

Figure 15 shows the full length DNA (17253 bp) and protein sequence (5742 aas) of the HIV Savine construct. Fragment boundaries are shown, together with the position of each fragment in each designed HIV protein, fragment number (in brackets), spacer 15 residues (two alanine residues) and which fragment the spacer was for (open boxes and arrows). The location of residual restriction site joining sequences corresponding to subcassette or cassette boundaries (shaded boxes) are also shown, along with start and stop codons, Kozak sequence, the location of the murine influenza virus CTL epitope sequence (near the 3' end), important restriction sites at each end and the position of each degenerate amino acid (indicated by 'X').

Figure 16 depicts the layout and position of oligonucleotides in the designed DNA sequence for subcassette A1. The sequences which annual to the short amplification oligonucleotides are indicated by hatched boxes and the position of oligonucleotide overlap regions are dark shaded.

Figure 17: Panel (a) depicts the stepwise asymmetric PCR of the two halves of subcassette A1 (lanes 2-5 and 7-9, respectively) and final splicing together by SOEing (lane 10). DNA standards in lane 1 are pUC18 digested with Sau3AI. Panel (b) shows the stepwise ligation-mediated joining and PCR amplification of each cassette as indicated. DNA standards in lane 1 are SPP1 cut with EcoRI.

30 Figure 18: Panel (a) shows summary of the construction of the DNA vaccine plasmids that express one HIV Savine cassette. Panel (b) shows a summary of the

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construction of the plasmids used for marker rescue recombination to generate Vaccinia viruses expressing one HIV Savine cassette. Panel (c) shows a summary of the construction of the DNA vaccine plasmids which each express a version of the full-length HIV Savine cDNA

Figure 19 shows restimulation of HIV specific polyclonal CTL responses from three HIV-infected patients by the HIV Savine constructs. PBMCs from three different patients were restimulated for 7 days by infection with Vaccinia virus pools expressing the HIV Savine cassettes: Pool 1 included VV-AC1 and VV-BC1; Pool 2 included VV-AC2, VV-BC2 and VV-CC2. The restimulated PBMCs were then mixed with autologous LCLs (effector to target ratio of 50:1), which were either uninfected or infected with either Vaccinia viruses expressing the HIV proteins gag (VV-gag), env (VV-env) or pol (VV-pol), VV-HIV Savine pools 1 (light bars) or 2 (dark bars) or a control Vaccinia virus (VV-Lac) and the amount of <sup>51</sup>Cr released used to determine percent specific lysis. K562 cells were used to determine the level of NK cell-mediated killing in their stimulated culture.

Figure 20 is a diagrammatic representation showing CD4+ proliferation of PBMCs from HIV-1 infected patients restimulated with either Pool1 or Pool2 of the HIV-1 Savine. Briefly PBMCs were stained with CFSE and culture for 6 days with or without VVs encoding either pool1 or pool2 of the HIV-1 Savine. Restimulated Cells were then labelled with antibodies and analysed by FACS.

Figure 21 is a graphical representation showing the CTL response in mice vaccinated with the HIV Savine. C57BL6 mice were immunised with the HIV-1 Savine DNA vaccine comprising the six plasmids described in Figure 18a (100 μg total DNA was given as 50 μg/leg i.m.). One week later Poxviruses (1x10<sup>7</sup> pfu) comprising Pool 1 of the HIV-1 Savine were used to boost the immune responses. Three weeks later splenocytes from these mice were restimulated with VV-Pool 1 or VV-Pool 2 for 5 days and the resultant effectors used in a <sup>51</sup>Cr release cytotoxicity assay against targets infected with CTRVV, VV-pools or VV expressing the natural antigens from HIV-1.

Figure 22 shows immune responses of HIV Immune Macaques (vaccinated with recombinant FPV expressing gag-pol and challenged with HIV-1 2 years prior to experiment). Monkeys 1 and 2 were immunised once at day 0 with VV Savine pool 1 (Three VVs which together express the entire HIV Savine ). Monkey 3 was immunised

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twice with FPV-gag-pol *i.e.*, Day 0 is 3 weeks after first FPV-gag-pol immunisation. A) IFN-y detection by ELISPOT of whole blood (0.5 mL, venous blood heparinanticoagulated) stimulated with Aldrithiol-2 inactivated whole HIV-1 (20 hours, 20 μg/mL). Plasma samples were then centrifuged (1000xg) and assayed in duplicate for antigen-specific IFN using capture ELISA. B) Flow cytometric detection of HIV-1 specific CD69+/CD8+ T cells. Freshly isolated PBMCs were stimulated with inactivated HIV-1 as above for 16 hours, washed and labelled with the antibodies. Cells were then analysed using a FACScalibur<sup>TM</sup> flow cytometer and data. analysed using Cell-Quest software. C) Flow cytometric detection of HIV-1 specific CD69+/CD4+ T cells carried out as in B).

Figure 23 shows a diagram of a system used to carry out the instructions encoded by the storage medium of Figures 28 and 29.

Figure 24 depicts a flow diagram showing an embodiment of a method for designing synthetic polynucleotide and synthetic polypeptides of the invention.

Figure 25 shows an algorithm, which *inter alia* utilises the steps of the method shown in Figure 24.

Figure 26 shows an example of applying the algorithm of Figure 25 to an input consensus polyprotein sequence of Hepatitis C 1a to execute the segmentation of the polyprotein sequence, the rearrangement of the segments, the linkage of the rearranged segments and the outputting of synthetic polynucleotide and polypeptide sequences for the preparation of Savines for treating and/or preventing Hepatitis C infection.

Figure 27 illustrates an example of applying the algorithm of Figure 25 to input consensus melanocyte differentiation antigens (gp100, MART, TRP-1, Tyros, Trp-2, MC1R, MUC1F and MUC1R) and to consensus melanoma specific antigens (BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b and LAGE1) to facilitate segmentation of those sequences, to rearrange the segments, to link the rearranged segments and to synthetic polynucleotide and polypeptide sequences for the preparation of Savines for treating and/or preventing melanoma.

Figure 28 shows a cross section of a magnetic storage medium.

Figure 29 shows a cross section of an optically readable data storage medium.

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Figure 30 shows six HIV Savine cassette sequences (A1 [SEQ ID NO: 393], A2 [SEQ ID NO: 399], B1[SEQ ID NO: 395], B2 [SEQ ID NO: 401], C1 [SEQ ID NO: 397] and C2 [SEQ ID NO: 403]). A1, B1 and C1 can be joined together using, for example, convenient restriction enzyme sites provided at the ends of each cassette to construct an embodiment of a full length HIV Savine [SEQ ID NO: 405]. A2, B2 and C2 can also be joined together to provide another embodiment of a full length HIV Savine with 350 aa mutations common in major HIV clades. The cassettes A/B/C can be joined into single constructs using specific restriction enzyme sites incorporated after the start codon or before the stop codon in the cassettes

### BRIEF DESCRIPTION OF THE SEQUENCES: SUMMARY TABLE

### TABLE A

SEQUENCE ID	SEQUENCE	LIINGTH
NUMBER		
SEQ ID NO: 1	GAG consensus polypeptide	499 aa
SEQ ID NO: 2	POL consensus polypeptide	995 aa
SEQ ID NO: 3	VIF consensus polypeptide	192 aa
SEQ ID NO: 4	VPR consensus polypeptide	96 aa
SEQ ID NO: 5	TAT consensus polypeptide	102 aa
SEQ ID NO: 6	REV consensus polypeptide	123 aa
SEQ ID NO: 7	VPU consensus polypeptide	81 aa
SEQ ID NO: 8	ENV consensus polypeptide	651 aa
SEQ ID NO: 9	NEF consensus polypeptide	206 aa
SEQ ID NO: 10	GAG segment 1	90 nts
SEQ ID NO: 11	Polypeptide encoded by SEQ ID NO: 10	30 aa
SEQ ID NO: 12	GAG segment 2	90 nts
SEQ ID NO: 13	Polypeptide encoded by SEQ ID NO: 12	30 aa
SEQ ID NO: 14	GAG segment 3	90 nts
SEQ ID NO: 15	Polypeptide encoded by SEQ ID NO: 14	30 aa
SEQ ID NO: 16	GAG segment 4	90 nts
SEQ ID NO: 17	Polypeptide encoded by SEQ ID NO: 16	30 aa
SEQ ID NO: 18	GAG segment 5	90 nts
SEQ ID NO: 19	Polypeptide encoded by SEQ ID NO: 18	30 aa
SEQ ID NO: 20	GAG segment 6	90 nts
SEQ ID NO: 21	Polypeptide encoded by SEQ ID NO: 20	30 aa
SEQ ID NO: 22	GAG segment 7	90 nts

SEQUENCE ID	SEQUENCE	TO THE WAY THE
NUMBER		LENGTH
SEQ ID NO: 23	Polypeptide encoded by SEQ ID NO: 22	30 aa
SEQ ID NO: 24	GAG segment 8	90 nts
SEQ ID NO: 25	Polypeptide encoded by SEQ ID NO: 24	30 aa
SEQ ID NO: 26	GAG segment 9	90 nts
SEQ ID NO: 27	Polypeptide encoded by SEQ ID NO: 26	30 aa
SEQ ID NO: 28	GAG segment 10	90 nts
SEQ ID NO: 29	Polypeptide encoded by SEQ ID NO: 28	30 aa
SEQ ID NO: 30	GAG segment 11	90 nts
SEQ ID NO: 31	Polypeptide encoded by SEQ ID NO: 30	30 aa
SEQ ID NO: 32	GAG segment 12	90 nts
SEQ ID NO: 33	Polypeptide encoded by SEQ ID NO: 32	30 aa
SEQ ID NO: 34	GAG segment 13	90 nts
SEQ ID NO: 35	Polypeptide encoded by SEQ ID NO: 34	30 aa
SEQ ID NO: 36	GAG segment 14	90 nts
SEQ ID NO: 37	Polypeptide encoded by SEQ ID NO: 36	30 aa
SEQ ID NO: 38	GAG segment 15	90 nts
SEQ ID NO: 39	Polypeptide encoded by SEQ ID NO: 38	30 aa
SEQ ID NO: 40	GAG segment 16	90 nts
SEQ ID NO: 41	Polypeptide encoded by SEQ ID NO: 40	30 aa
SEQ ID NO: 42	GAG segment 17	90 nts
SEQ ID NO: 43	Polypeptide encoded by SEQ ID NO: 42	30 aa
SEQ ID NO: 44	GAG segment 18	90 nts
SEQ ID NO: 45	Polypeptide encoded by SEQ ID NO: 44	30 aa
SEQ ID NO: 46	GAG segment 19	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 47	Polypeptide encoded by SEQ ID NO: 46	30 aa
SEQ ID NO: 48	GAG segment 20	90 nts
SEQ ID NO: 49	Polypeptide encoded by SEQ ID NO: 48	30 aa
SEQ ID NO: 50	GAG segment 21	90 nts
SEQ ID NO: 51	Polypeptide encoded by SEQ ID NO: 50	30 aa
SEQ ID NO: 52	GAG segment 22	90 nts
SEQ ID NO: 53	Polypeptide encoded by SEQ ID NO: 52	30 aa
SEQ ID NO: 54	GAG segment 23	90 nts
SEQ ID NO: 55	Polypeptide encoded by SEQ ID NO: 54	30 aa
SEQ ID NO: 56	GAG segment 24	90 nts
SEQ ID NO: 57	Polypeptide encoded by SEQ ID NO: 56	30 aa
SEQ ID NO: 58	GAG segment 25	90 nts
SEQ ID NO: 59	Polypeptide encoded by SEQ ID NO: 58	30 aa
SEQ ID NO: 60	GAG segment 26	90 nts
SEQ ID NO: 61	Polypeptide encoded by SEQ ID NO: 60	30 aa
SEQ ID NO: 62	GAG segment 27	90 nts
SEQ ID NO: 63	Polypeptide encoded by SEQ ID NO: 62	30 aa
SEQ ID NO: 64	GAG segment 28	90 nts
SEQ ID NO: 65	Polypeptide encoded by SEQ ID NO: 64	30 aa
SEQ ID NO: 66	GAG segment 29	90 nts
SEQ ID NO: 67	Polypeptide encoded by SEQ ID NO: 66	30 aa
SEQ ID NO: 68	GAG segment 30	90 nts
SEQ ID NO: 69	Polypeptide encoded by SEQ ID NO: 68	30 aa
SEQ ID NO: 70	GAG segment 31	90 nts

SEQUENCE IID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 71	Polypeptide encoded by SEQ ID NO: 70	30 aa
SEQ ID NO: 72	GAG segment 32	90 nts
SEQ ID NO: 73	Polypeptide encoded by SEQ ID NO: 72	30 aa
SEQ ID NO: 74	GAG segment 33	57 nts
SEQ ID NO: 75	Polypeptide encoded by SEQ ID NO: 74	19 aa
SEQ ID NO: 76	POL segment 1	90 nts
SEQ ID NO: 77	Polypeptide encoded by SEQ ID NO: 76	30 aa
SEQ ID NO: 78	POL segment 2	90 nts
SEQ ID NO: 79	Polypeptide encoded by SEQ ID NO: 78	30 aa
SEQ ID NO: 80	POL segment 3	90 nts
SEQ ID NO: 81	Polypeptide encoded by SEQ ID NO: 80	30 aa
SEQ ID NO: 82	POL segment 4	90 nts
SEQ ID NO: 83	Polypeptide encoded by SEQ ID NO: 82	30 aa
SEQ ID NO: 84	POL segment 5	90 nts
SEQ ID NO: 85	Polypeptide encoded by SEQ ID NO: 84	30 aa
SEQ ID NO: 86	POL segment 6	90 nts
SEQ ID NO: 87	Polypeptide encoded by SEQ ID NO: 86	30 aa
SEQ ID NO: 88	POL segment 7	90 nts
SEQ ID NO: 89	Polypeptide encoded by SEQ ID NO: 88	30 aa
SEQ ID NO: 90	POL segment 8	90 nts
SEQ ID NO: 91	Polypeptide encoded by SEQ ID NO: 90	30 aa
SEQ ID NO: 92	POL segment 9	90 nts
SEQ ID NO: 93	Polypeptide encoded by SEQ ID NO: 92	30 aa
SEQ ID NO: 94	POL segment 10	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 95	Polypeptide encoded by SEQ ID NO: 94	30 aa
SEQ ID NO: 96	POL segment 11	90 nts
SEQ ID NO: 97	Polypeptide encoded by SEQ ID NO: 96	30 aa
SEQ ID NO: 98	POL segment 12	90 nts
SEQ ID NO: 99	Polypeptide encoded by SEQ ID NO: 98	30 aa
SEQ ID NO: 100	POL segment 13	90 nts
SEQ ID NO: 101	Polypeptide encoded by SEQ ID NO: 100	30 aa
SEQ ID NO: 102	POL segment 14	90 nts
SEQ ID NO: 103	Polypeptide encoded by SEQ ID NO: 102	30 aa
SEQ ID NO: 104	POL segment 15	90 nts
SEQ ID NO: 105	Polypeptide encoded by SEQ ID NO: 104	30 aa
SEQ ID NO: 106	POL segment 16	90 nts
SEQ ID NO: 107	Polypeptide encoded by SEQ ID NO: 106	30 aa
SEQ ID NO: 108	POL segment 17	90 nts
SEQ ID NO: 109	Polypeptide encoded by SEQ ID NO: 108	30 aa
SEQ ID NO: 110	POL segment 18	90 nts
SEQ ID NO: 111	Polypeptide encoded by SEQ ID NO: 110	30 aa
SEQ ID NO: 112	POL segment 19	90 nts
SEQ ID NO: 113	Polypeptide encoded by SEQ ID NO: 112	30 aa
SEQ ID NO: 114	POL segment 20	90 nts
SEQ ID NO: 115	Polypeptide encoded by SEQ ID NO: 114	30 aa
SEQ ID NO: 116	POL segment 21	90 nts
SEQ ID NO: 117	Polypeptide encoded by SEQ ID NO: 116	30 aa
SEQ ID NO: 118	POL segment 22	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 119	Polypeptide encoded by SEQ ID NO: 118	30 aa
SEQ ID NO: 120	POL segment 23	90 nts
SEQ ID NO: 121	Polypeptide encoded by SEQ ID NO: 120	30 aa
SEQ ID NO: 122	POL segment 24	90 nts
SEQ ID NO: 123	Polypeptide encoded by SEQ ID NO: 122	30 aa
SEQ ID NO: 124	POL segment 25	90 nts
SEQ ID NO: 125	Polypeptide encoded by SEQ ID NO: 124	30 aa
SEQ ID NO: 126	POL segment 26	90 nts
SEQ ID NO: 127	Polypeptide encoded by SEQ ID NO: 126	30 aa
SEQ ID NO: 128	POL segment 27	90 nts
SEQ ID NO: 129	Polypeptide encoded by SEQ ID NO: 128	30 aa
SEQ ID NO: 130	POL segment 28	90 nts
SEQ ID NO: 131	Polypeptide encoded by SEQ ID NO: 130	30 aa
SEQ ID NO: 132	POL segment 29	90 nts
SEQ ID NO: 133	Polypeptide encoded by SEQ ID NO: 132	30 aa
SEQ ID NO: 134	POL segment 30	90 nts
SEQ ID NO: 135	Polypeptide encoded by SEQ ID NO: 134	30 aa
SEQ ID NO: 136	POL segment 31	90 nts
SEQ ID NO: 137	Polypeptide encoded by SEQ ID NO: 136	30 aa
SEQ ID NO: 138	POL segment 32	90 nts
SEQ ID NO: 139	Polypeptide encoded by SEQ ID NO: 138	30 aa
SEQ ID NO: 140	POL segment 33	90 nts
SEQ ID NO: 141	Polypeptide encoded by SEQ ID NO: 140	30 aa
SEQ ID NO: 142	POL segment 34	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 143	Polypeptide encoded by SEQ ID NO: 142	30 aa
SEQ ID NO: 144	POL segment 35	90 nts
SEQ ID NO: 145	Polypeptide encoded by SEQ ID NO: 144	30 aa
SEQ ID NO: 146	POL segment 36	90 nts
SEQ ID NO: 147	Polypeptide encoded by SEQ ID NO: 146	30 aa
SEQ ID NO: 148	POL segment 37	90 nts
SEQ ID NO: 149	Polypeptide encoded by SEQ ID NO: 148	30 aa
SEQ ID NO: 150	POL segment 38	90 nts
SEQ ID NO: 151	Polypeptide encoded by SEQ ID NO: 150	30 aa
SEQ ID NO: 152	POL segment 39	90 nts
SEQ ID NO: 153	Polypeptide encoded by SEQ ID NO: 152	30 aa
SEQ ID NO: 154	POL segment 40	90 nts
SEQ ID NO: 155	Polypeptide encoded by SEQ ID NO: 154	30 aa
SEQ ID NO: 156	POL segment 41	90 nts
SEQ ID NO: 157	Polypeptide encoded by SEQ ID NO: 156	30 aa
SEQ ID NO: 158	POL segment 42	90 nts
SEQ ID NO: 159	Polypeptide encoded by SEQ ID NO: 158	30 aa
SEQ ID NO: 160	POL segment 43	90 nts
SEQ ID NO: 161	Polypeptide encoded by SEQ ID NO: 160	30 aa
SEQ ID NO: 162	POL segment 44	90 nts
SEQ ID NO: 163	Polypeptide encoded by SEQ ID NO: 162	30 aa
SEQ ID NO: 164	POL segment 45	90 nts
SEQ ID NO: 165	Polypeptide encoded by SEQ ID NO: 164	30 aa
SEQ ID NO: 166	POL segment 46	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 167	Polypeptide encoded by SEQ ID NO: 166	30 aa
SEQ ID NO: 168	POL segment 47	90 nts
SEQ ID NO: 169	Polypeptide encoded by SEQ ID NO: 168	30 aa
SEQ ID NO: 170	POL segment 48	90 nts
SEQ ID NO: 171	Polypeptide encoded by SEQ ID NO: 170	30 aa
SEQ ID NO: 172	POL segment 49	90 nts
SEQ ID NO: 173	Polypeptide encoded by SEQ ID NO: 172	30 aa
SEQ ID NO: 174	POL segment 50	90 nts
SEQ ID NO: 175	Polypeptide encoded by SEQ ID NO: 174	30 aa
<b>SEQ ID NO: 176</b>	POL segment 51	90 nts
SEQ ID NO: 177	Polypeptide encoded by SEQ ID NO: 176	30 aa
SEQ ID NO: 178	POL segment 52	90 nts
SEQ ID NO: 179	Polypeptide encoded by SEQ ID NO: 178	30 aa
SEQ ID NO: 180	POL segment 53	90 nts
SEQ ID NO: 181	Polypeptide encoded by SEQ ID NO: 180	30 aa
SEQ ID NO: 182	POL segment 54	90 nts
SEQ ID NO: 183	Polypeptide encoded by SEQ ID NO: 182	30 aa
SEQ ID NO: 184	POL segment 55	90 nts
SEQ ID NO: 185	Polypeptide encoded by SEQ ID NO: 184	30 aa
SEQ ID NO: 186	POL segment 56	90 nts
SEQ ID NO: 187	Polypeptide encoded by SEQ ID NO: 186	·30 aa
SEQ ID NO: 188	POL segment 57	90 nts
SEQ ID NO: 189	Polypeptide encoded by SEQ ID NO: 188	30 aa
SEQ ID NO: 190	POL segment 58	90 nts

SEQUENCE ID NUMBER	NEQUENCE	LENGTH
SEQ ID NO: 191	Polypeptide encoded by SEQ ID NO: 190	30 aa
SEQ ID NO: 192	POL segment 59	90 nts
SEQ ID NO: 193	Polypeptide encoded by SEQ ID NO: 192	30 aa
SEQ ID NO: 194	POL segment 60	90 nts
SEQ ID NO: 195	Polypeptide encoded by SEQ ID NO: 194	30 aa
SEQ ID NO: 196	POL segment 61	90 nts
SEQ ID NO: 197	Polypeptide encoded by SEQ ID NO: 196	30 aa ·
SEQ ID NO: 198	POL segment 62	90 nts
SEQ ID NO: 199	Polypeptide encoded by SEQ ID NO: 198	30 aa
SEQ ID NO: 200	POL segment 63	90 nts
SEQ ID NO: 201	Polypeptide encoded by SEQ ID NO: 200	30 aa
SEQ ID NO: 202	POL segment 64	90 nts
SEQ ID NO: 203	Polypeptide encoded by SEQ ID NO: 202	30 aa
SEQ ID NO: 204	POL segment 65	90 nts
SEQ ID NO: 205	Polypeptide encoded by SEQ ID NO: 204	30 aa
SEQ ID NO: 206	POL segment 66	60 nts
SEQ ID NO: 207	Polypeptide encoded by SEQ ID NO: 206	20 aa <sub>.</sub>
SEQ ID NO: 208	VIF segment 1	90 nts
SEQ ID NO: 209	Polypeptide encoded by SEQ ID NO: 208	30 aa
SEQ ID NO: 210	VIF segment 2	90 nts
SEQ ID NO: 211	Polypeptide encoded by SEQ ID NO: 210	30 aa
SEQ ID NO: 212	VIF segment 3	90 nts
SEQ ID NO: 213	Polypeptide encoded by SEQ ID NO: 212	30 aa
SEQ ID NO: 214	VIF segment 4	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH :
SEQ ID NO: 215	Polypeptide encoded by SEQ ID NO: 214	30 aa
SEQ ID NO: 216	VIF segment 5	90 nts
SEQ ID NO: 217	Polypeptide encoded by SEQ ID NO: 216	30 aa
SEQ ID NO: 218	VIF segment 6	90 nts
SEQ ID NO: 219	Polypeptide encoded by SEQ ID NO: 218	30 aa
SEQ ID NO: 220	VIF segment 7	90 nts
SEQ ID NO: 221	Polypeptide encoded by SEQ ID NO: 220	30 aa
SEQ ID NO: 222	VIF segment 8	90 nts
SEQ ID NO: 223	Polypeptide encoded by SEQ ID NO: 222	30 aa
SEQ ID NO: 224	VIF segment 9	90 nts
SEQ ID NO: 225	Polypeptide encoded by SEQ ID NO: 224	30 aa
SEQ ID NO: 226	VIF segment 10	90 nts
SEQ ID NO: 227	Polypeptide encoded by SEQ ID NO: 226	30 aa
SEQ ID NO: 228	VIF segment 11	90 nts
SEQ ID NO: 229	Polypeptide encoded by SEQ ID NO: 228	30 aa
SEQ ID NO: 230	VIF segment 12	81 nts
<b>SEQ ID NO: 231</b>	Polypeptide encoded by SEQ ID NO: 230	27 aa
<b>SEQ ID NO: 232</b>	VPR segment 1	90 nts
SEQ ID NO: 233	Polypeptide encoded by SEQ ID NO: 232	30 aa
<b>SEQ ID NO: 234</b>	VPR segment 2	90 nts
<b>SEQ ID NO: 235</b>	Polypeptide encoded by SEQ ID NO: 234	30 aa
SEQ ID NO: 236	VPR segment 3	90 nts
<b>SEQ ID NO: 237</b>	Polypeptide encoded by SEQ ID NO: 236	30 aa
SEQ ID NO: 238	VPR segment 4	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 239	Polypeptide encoded by SEQ ID NO: 238	30 aa
SEQ ID NO: 240	VPR segment 5	90 nts
SEQ ID NO: 241	Polypeptide encoded by SEQ ID NO: 240	30 aa
SEQ ID NO: 242	VPR segment 6	63 nts
SEQ ID NO: 243	Polypeptide encoded by SEQ ID NO: 242	21 aa
SEQ ID NO: 244	TAT segment 1	90 nts
SEQ ID NO: 245	Polypeptide encoded by SEQ ID NO: 244	30 aa
SEQ ID NO: 246	TAT segment 2	90 nts
SEQ ID NO: 247	Polypeptide encoded by SEQ ID NO: 246	30 aa
SEQ ID NO: 248	TAT segment 3	90 nts
SEQ ID NO: 249	Polypeptide encoded by SEQ ID NO: 248	30 aa
SEQ ID NO: 250	TAT segment 4	90 nts
SEQ ID NO: 251	Polypeptide encoded by SEQ ID NO: 250	30 aa
SEQ ID NO: 252	TAT segment 5	90 nts
<b>SEQ ID NO: 253</b>	Polypeptide encoded by SEQ ID NO: 252	30 aa
SEQ ID NO: 254	TAT segment 6	81 nts
<b>SEQ ID NO: 255</b>	Polypeptide encoded by SEQ ID NO: 254	27 aa
<b>SEQ ID NO: 256</b>	REV segment 1	90 nts
<b>SEQ ID NO: 257</b>	Polypeptide encoded by SEQ ID NO: 256	30 aa
<b>SEQ ID NO: 258</b>	REV segment 2	90 nts
SEQ ID NO: 259	Polypeptide encoded by SEQ ID NO: 258	30 aa
SEQ ID NO: 260	REV segment 3	90 nts
SEQ ID NO: 261	Polypeptide encoded by SEQ ID NO: 260	30 aa
SEQ ID NO: 262	REV segment 4	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 263	Polypeptide encoded by SEQ ID NO: 262	30 aa
SEQ ID NO: 264	REV segment 5	90 nts
SEQ ID NO: 265	Polypeptide encoded by SEQ ID NO: 264	30 aa
SEQ ID NO: 266	REV segment 6	90 nts
SEQ ID NO: 267	Polypeptide encoded by SEQ ID NO: 266	30 aa
SEQ ID NO: 268	REV segment 7	90 nts
SEQ ID NO: 269	Polypeptide encoded by SEQ ID NO: 268	30 aa
SEQ ID NO: 270	REV segment 8	54 nts
SEQ ID NO: 271	Polypeptide encoded by SEQ ID NO: 270	18 aa
SEQ ID NO: 272	VPU segment 1	90 nts
SEQ ID NO: 273	Polypeptide encoded by SEQ ID NO: 272	30 aa
SEQ ID NO: 274	VPU segment 2	90 nts
SEQ ID NO: 275	Polypeptide encoded by SEQ ID NO: 274	30 aa
SEQ ID NO: 276	VPU segment 3	90 nts
SEQ ID NO: 277	Polypeptide encoded by SEQ ID NO: 276	30 aa
SEQ ID NO: 278	VPU segment 4	90 nts
SEQ ID NO: 279	Polypeptide encoded by SEQ ID NO: 278	30 aa
SEQ ID NO: 280	VPU segment 5	63 nts
SEQ ID NO: 281	Polypeptide encoded by SEQ ID NO: 280	21 aa
SEQ ID NO: 282	ENV segment 1	90 nts
SEQ ID NO: 283	Polypeptide encoded by SEQ ID NO: 282	30 aa
SEQ ID NO: 284	ENV segment 2	90 nts
SEQ ID NO: 285	Polypeptide encoded by SEQ ID NO: 284	30 aa
SEQ ID NO: 286	ENV segment 3	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 287	Polypeptide encoded by SEQ ID NO: 286	30 aa
SEQ ID NO: 288	ENV segment 4	90 nts
SEQ ID NO: 289	Polypeptide encoded by SEQ ID NO: 288	30 aa
SEQ ID NO: 290	ENV segment 5	90 nts
SEQ ID NO: 291	Polypeptide encoded by SEQ ID NO: 290	30 aa
SEQ ID NO: 292	ENV segment 6	90 nts
SEQ ID NO: 293	Polypeptide encoded by SEQ ID NO: 292	30 aa
SEQ ID NO: 294	ENV segment 7	90 nts
SEQ ID NO: 295	Polypeptide encoded by SEQ ID NO: 294	30 aa
SEQ ID NO: 296	ENV segment 8	90 nts
SEQ ID NO: 297	Polypeptide encoded by SEQ ID NO: 296	30 aa
SEQ ID NO: 298	ENV segment 9	57 nts
SEQ ID NO: 299	Polypeptide encoded by SEQ ID NO: 298	19 aa
SEQ ID NO: 300	GAP A segment 1	90 nts
SEQ ID NO: 301	Polypeptide encoded by SEQ ID NO: 300	30 aa
SEQ ID NO: 302	GAP A segment 2	90 nts
SEQ ID NO: 303	Polypeptide encoded by SEQ ID NO: 302	30 aa
SEQ ID NO: 304	GAP A segment 3	90 nts
SEQ ID NO: 305	Polypeptide encoded by SEQ ID NO: 304	30 aa
SEQ ID NO: 306	GAP A segment 4	90 nts
SEQ ID NO: 307	Polypeptide encoded by SEQ ID NO: 306	30 aa
SEQ ID NO: 308	GAP A segment 5	90 nts
SEQ ID NO: 309	Polypeptide encoded by SEQ ID NO: 308	30 aa
SEQ ID NO: 310	GAP A segment 6	90 nts

SEQUENCE ID NUMBER	SECUENCE	LENGTH
SEQ ID NO: 311	Polypeptide encoded by SEQ ID NO: 310	30 aa
SEQ ID NO: 312	GAP A segment 7	75 nts
SEQ ID NO: 313	Polypeptide encoded by SEQ ID NO: 312	25 nts
SEQ ID NO: 314	GAP B segment 1	90 nts
SEQ ID NO: 315	Polypeptide encoded by SEQ ID NO: 314	30 aa
SEQ ID NO: 316	GAP B segment 2	90 nts
SEQ ID NO: 317	Polypeptide encoded by SEQ ID NO: 316	30 aa
SEQ ID NO: 318	GAP B segment 3	90 nts
SEQ ID NO: 319	Polypeptide encoded by SEQ ID NO: 318	30 aa
SEQ ID NO: 320	GAP B segment 4	90 nts
SEQ ID NO: 321	Polypeptide encoded by SEQ ID NO: 320	30 aa
SEQ ID NO: 322	GAP B segment 5	90 nts
SEQ ID NO: 323	Polypeptide encoded by SEQ ID NO: 322	30 aa
SEQ ID NO: 324	GAP B segment 6	90 nts
SEQ ID NO: 325	Polypeptide encoded by SEQ ID NO: 324	30 aa
SEQ ID NO: 326	GAP B segment 7	90 nts
SEQ ID NO: 327	Polypeptide encoded by SEQ ID NO: 326	30 aa
SEQ ID NO: 328	GAP B segment 8	90 nts
SEQ ID NO: 329	Polypeptide encoded by SEQ ID NO: 328	30 aa
SEQ ID NO: 330	GAP B segment 9	90 nts
SEQ ID NO: 331	Polypeptide encoded by SEQ ID NO: 330	30 aa
SEQ ID NO: 332	GAP B segment 10	90 nts
SEQ ID NO: 333	Polypeptide encoded by SEQ ID NO: 332	30 aa
SEQ ID NO: 334	GAP B segment 11	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 335	Polypeptide encoded by SEQ ID NO: 334	30 aa
SEQ ID NO: 336	GAP B segment 12	90 nts .
SEQ ID NO: 337	Polypeptide encoded by SEQ ID NO: 336	30 aa
SEQ ID NO: 338	GAP B segment 13	90 nts
SEQ ID NO: 339	Polypeptide encoded by SEQ ID NO: 338	30 aa
SEQ ID NO: 340	GAP B segment 14	90 nts
SEQ ID NO: 341	Polypeptide encoded by SEQ ID NO: 340	30 aa
SEQ ID NO: 342	GAP B segment 15	90 nts
SEQ ID NO: 343	Polypeptide encoded by SEQ ID NO: 342	30 aa
SEQ ID NO: 344	GAP B segment 16	90 nts
SEQ ID NO: 345	Polypeptide encoded by SEQ ID NO: 344	30 aa
SEQ ID NO: 346	GAP B segment 17	90 nts
SEQ ID NO: 347	Polypeptide encoded by SEQ ID NO: 346	30 aa
SEQ ID NO: 348	GAP B segment 18	90 nts
SEQ ID NO: 349	Polypeptide encoded by SEQ ID NO: 348	30 aa
SEQ ID NO: 350	GAP B segment 19	90 nts
SEQ ID NO: 351	Polypeptide encoded by SEQ ID NO: 350	30 aa
<b>SEQ ID NO: 352</b>	GAP B segment 20	90 nts
SEQ ID NO: 353	Polypeptide encoded by SEQ ID NO: 352	30 aa
SEQ ID NO: 354	GAP B segment 21	90 nts
SEQ ID NO: 355	Polypeptide encoded by SEQ ID NO: 354	30 aa
SEQ ID NO: 356	GAP B segment 22	90 nts
SEQ ID NO: 357	Polypeptide encoded by SEQ ID NO: 356	30 aa
SEQ ID NO: 358	GAP B segment 23	90 nts

SEQUENCE ID	SEQUENCS	LENGTH
NUMBER		
SEQ ID NO: 359	Polypeptide encoded by SEQ ID NO: 358	30 aa
SEQ ID NO: 360	GAP B segment 24	90 nts
SEQ ID NO: 361	Polypeptide encoded by SEQ ID NO: 360	30 aa
SEQ ID NO: 362	GAP B segment 25	90 nts
SEQ ID NO: 363	Polypeptide encoded by SEQ ID NO: 362	30 aa
SEQ ID NO: 364	GAP B segment 26	66 nts
<b>SEQ ID NO: 365</b>	Polypeptide encoded by SEQ ID NO: 364	22 aa
SEQ ID NO: 366	NEF segment 1	90 nts
SEQ ID NO: 367	Polypeptide encoded by SEQ ID NO: 366	30 aa
SEQ ID NO: 368	NEF segment 2	90 nts
SEQ ID NO: 369	Polypeptide encoded by SEQ ID NO: 368	30 aa
SEQ ID NO: 370	NEF segment 3	90 nts
SEQ ID NO: 371	Polypeptide encoded by SEQ ID NO: 370	30 aa
SEQ ID NO: 372	NEF segment 4	90 nts
SEQ ID NO: 373	Polypeptide encoded by SEQ ID NO: 372	30 aa
<b>SEQ ID NO: 374</b>	NEF segment 5	90 nts
<b>SEQ ID NO: 375</b>	Polypeptide encoded by SEQ ID NO: 374	30 aa
<b>SEQ ID NO: 376</b>	NEF segment 6	90 nts
SEQ ID NO: 377	Polypeptide encoded by SEQ ID NO: 376	30 aa
SEQ ID NO: 378	NEF segment 7	90 nts
SEQ ID NO: 379	Polypeptide encoded by SEQ ID NO: 378	30 aa
SEQ ID NO: 380	NEF segment 8	90 nts
SEQ ID NO: 381	Polypeptide encoded by SEQ ID NO: 380	30 aa
SEQ ID NO: 382	NEF segment 9	90 nts

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 383	Polypeptide encoded by SEQ ID NO: 382	30 aa
SEQ ID NO: 384	NEF segment 10	90 nts
SEQ ID NO: 385	Polypeptide encoded by SEQ ID NO: 384	30 aa
<b>SEQ ID NO: 386</b>	NEF segment 11	90 nts
SEQ ID NO: 387	Polypeptide encoded by SEQ ID NO: 386	30 aa
SEQ ID NO: 388	NEF segment 12	90 nts
SEQ ID NO: 389	Polypeptide encoded by SEQ ID NO: 388	30 aa
SEQ ID NO: 390	NEF segment 13	78 nts
SEQ ID NO: 391	Polypeptide encoded by SEQ ID NO: 390	26 aa
SEQ ID NO: 392	HIV Cassette A1	5703 nts
SEQ ID NO: 393	Polypeptide encoded by SEQ ID NO:392	1896 aa
SEQ ID NO: 394	HIV Cassette B1	5685 nts
SEQ ID NO: 395	Polypeptide encoded by SEQ ID NO: 394	1890 aa
SEQ ID NO: 396	HIV Cassette C1	5925 nts
SEQ ID NO: 397	Polypeptide encoded by SEQ ID NO: 396	1967 aa
SEQ ID NO: 398	HIV Cassette A2	5703 nts
SEQ ID NO: 399	Polypeptide encoded by SEQ ID NO: 398	1896 aa
SEQ ID NO: 400	HIV Cassette B2	5685 nts
SEQ ID NO: 401	Polypeptide encoded by SEQ ID NO: 400	1890 aa
SEQ ID NO: 402	HIV Cassette C2	5925 nts
SEQ ID NO: 403	Polypeptide encoded by SEQ ID NO: 402	1967 aa
SEQ ID NO: 404	HIV complete Savine	17244 nts
SEQ ID NO: 405	Polypeptide encoded by SEQ ID NO: 404	5747 aa
SEQ ID NO: 406	HepCla consensus polyprotein sequence	3011 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 407	HepCla segment 1	90 nts
SEQ ID NO: 408	Polypeptide encoded by SEQ ID NO: 407	30 aa
SEQ ID NO: 409	HepCla segment 2	90 nts
SEQ ID NO: 410	Polypeptide encoded by SEQ ID NO: 409	30 aa
SEQ ID NO: 411	HepCla segment 3	90 nts
SEQ ID NO: 412	Polypeptide encoded by SEQ ID NO: 411	30 aa
SEQ ID NO: 413	HepC1a segment 4	90 nts
SEQ ID NO: 414	Polypeptide encoded by SEQ ID NO: 413	30 aa
SEQ ID NO: 415	HepCla segment 5	90 nts
SEQ ID NO: 416	Polypeptide encoded by SEQ ID NO: 415	30 aa
SEQ ID NO: 417	HepCla segment 6	90 nts
SEQ ID NO: 418	Polypeptide encoded by SEQ ID NO: 417	30 aa
SEQ ID NO: 419	HepCla segment 7	90 nts
SEQ ID NO: 420	Polypeptide encoded by SEQ ID NO: 419	30 aa
SEQ ID NO: 421	HepCla segment 8	90 nts
SEQ ID NO: 422	Polypeptide encoded by SEQ ID NO: 421	30 aa
SEQ ID NO: 423	HepCla segment 9	90 nts
SEQ ID NO: 424	Polypeptide encoded by SEQ ID NO: 423	30 aa
SEQ ID NO: 425	HepCla segment 10	90 nts
SEQ ID NO: 426	Polypeptide encoded by SEQ ID NO: 425	30 aa
SEQ ID NO: 427	HepCla segment 11	90 nts
SEQ ID NO: 428	Polypeptide encoded by SEQ ID NO: 427	30 aa
SEQ ID NO: 429	HepC1a segment 12	90 nts
SEQ ID NO: 430	Polypeptide encoded by SEQ ID NO: 429	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 431	HepCla segment 13	90 nts
SEQ ID NO: 432	Polypeptide encoded by SEQ ID NO: 431	30 aa
SEQ ID NO: 433	HepCla segment 14	90 nts
SEQ ID NO: 434	Polypeptide encoded by SEQ ID NO: 433	30 aa
SEQ ID NO: 435	HepCla segment 15	90 nts
SEQ ID NO: 436	Polypeptide encoded by SEQ ID NO: 435	30 aa
SEQ ID NO: 437	HepC1a segment 16	90 nts
SEQ ID NO: 438	Polypeptide encoded by SEQ ID NO: 437	30 aa
SEQ ID NO: 439	HepCla segment 17	90 nts
SEQ ID NO: 440	Polypeptide encoded by SEQ ID NO: 439	30 aa
SEQ ID NO: 441	HepC1a segment 18	90 nts
SEQ ID NO: 442	Polypeptide encoded by SEQ ID NO: 441	30 aa
SEQ ID NO: 443	HepCla segment 19	90 nts
SEQ ID NO: 444	Polypeptide encoded by SEQ ID NO: 443	30 aa
SEQ ID NO: 445	HepCla segment 20	90 nts
SEQ ID NO: 446	Polypeptide encoded by SEQ ID NO: 445	30 aa
SEQ ID NO: 447	HepCla segment 21	90 nts
SEQ ID NO: 448	Polypeptide encoded by SEQ ID NO: 447	30 aa
SEQ ID NO: 449	HepC1a segment 22	90 nts
SEQ ID NO: 450	Polypeptide encoded by SEQ ID NO: 449	30 aa
SEQ ID NO: 451	HepCla segment 23	90 nts
SEQ ID NO: 452	Polypeptide encoded by SEQ ID NO: 451	30 aa
SEQ ID NO: 453	HepCla segment 24	90 nts
SEQ ID NO: 454	Polypeptide encoded by SEQ ID NO: 453	30 aa

SEQUENCE III) NUMBER	SEQUENCE	LENGINI
SEQ ID NO: 455	HepCla segment 25	90 nts
SEQ ID NO: 456	Polypeptide encoded by SEQ ID NO: 455	30 aa
SEQ ID NO: 457	HepCla segment 26	90 nts
SEQ ID NO: 458	Polypeptide encoded by SEQ ID NO: 457	30 aa
SEQ ID NO: 459	HepC1a segment 27	90 nts
SEQ ID NO: 460	Polypeptide encoded by SEQ ID NO: 459	30 aa
SEQ ID NO: 461	HepC1a segment 28	90 nts
SEQ ID NO: 462	Polypeptide encoded by SEQ ID NO: 461	30 aa
SEQ ID NO: 463	HepCla segment 29	90 nts
SEQ ID NO: 464	Polypeptide encoded by SEQ ID NO: 463	30 aa
SEQ ID NO: 465	HepC1a segment 30	90 nts
SEQ ID NO: 466	Polypeptide encoded by SEQ ID NO: 465	30 aa
SEQ ID NO: 467	HepCla segment 31	90 nts
SEQ ID NO: 468	Polypeptide encoded by SEQ ID NO: 467	30 aa
SEQ ID NO: 469	HepC1a segment 32	90 nts
SEQ ID NO: 470	Polypeptide encoded by SEQ ID NO: 469	30 aa
SEQ ID NO: 471	HepCla segment 33	90 nts
SEQ ID NO: 472	Polypeptide encoded by SEQ ID NO: 471	30 aa
SEQ ID NO: 473	HepCla segment 34	90 nts
SEQ ID NO: 474	Polypeptide encoded by SEQ ID NO: 473	30 aa
SEQ ID NO: 475	HepC1a segment 35	90 nts
SEQ ID NO: 476	Polypeptide encoded by SEQ ID NO: 475	30 aa
SEQ ID NO: 477	HepCla segment 36	90 nts
SEQ ID NO: 478	Polypeptide encoded by SEQ ID NO: 477	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 479	HepCla segment 37	90 nts
SEQ ID NO: 480	Polypeptide encoded by SEQ ID NO: 479	30 aa
SEQ ID NO: 481	HepC1a segment 38	90 nts
SEQ ID NO: 482	Polypeptide encoded by SEQ ID NO: 481	30 aa
SEQ ID NO: 483	HepCla segment 39	90 nts
SEQ ID NO: 484	Polypeptide encoded by SEQ ID NO: 483	30 aa
SEQ ID NO: 485	HepC1a segment 40	90 nts
SEQ ID NO: 486.	Polypeptide encoded by SEQ ID NO: 485	30 aa
SEQ ID NO: 487	HepCla segment 41	90 nts
SEQ ID NO: 488	Polypeptide encoded by SEQ ID NO: 487	30 aa
SEQ ID NO: 489	HepC1a segment 42	90 nts
SEQ ID NO: 490	Polypeptide encoded by SEQ ID NO: 489	30 aa
SEQ ID NO: 491	HepC1a segment 43	90 nts
SEQ ID NO: 492	Polypeptide encoded by SEQ ID NO: 491	30 aa
SEQ ID NO: 493	HepCla segment 44	90 nts
SEQ ID NO: 494	Polypeptide encoded by SEQ ID NO: 493	30 aa
SEQ ID NO: 495	HepC1a segment 45	90 nts
SEQ ID NO: 496	Polypeptide encoded by SEQ ID NO: 495	30 aa
SEQ ID NO: 497	HepCla segment 46	90 nts
SEQ ID NO: 498	Polypeptide encoded by SEQ ID NO: 497	30 aa
SEQ ID NO: 499	HepCla segment 47	90 nts
SEQ ID NO: 500	Polypeptide encoded by SEQ ID NO: 499	30 aa
SEQ ID NO: 501	HepCla segment 48	90 nts
<b>SEQ ID NO: 502</b>	Polypeptide encoded by SEQ ID NO: 501	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LIENGTH
SEQ ID NO: 503	HepCla segment 49	90 nts
SEQ ID NO: 504	Polypeptide encoded by SEQ ID NO: 503	30 aa
SEQ ID NO: 505	HepC1a segment 50	90 nts
SEQ ID NO: 506	Polypeptide encoded by SEQ ID NO: 505	30 aa
SEQ ID NO: 507	HepCla segment 51	90 nts
SEQ ID NO: 508	Polypeptide encoded by SEQ ID NO: 507	30 aa
SEQ ID NO: 509	HepC1a segment 52	90 nts
SEQ ID NO: 510	Polypeptide encoded by SEQ ID NO: 509	30 aa
SEQ ID NO: 511	HepC1a segment 53	90 nts
SEQ ID NO: 512	Polypeptide encoded by SEQ ID NO: 511	30 aa
SEQ ID NO: 513	HepC1a segment 54	90 nts
SEQ ID NO: 514	Polypeptide encoded by SEQ ID NO: 513	30 aa
SEQ ID NO: 515	HepC1a segment 55	90 nts
SEQ ID NO: 516	Polypeptide encoded by SEQ ID NO: 515	30 aa
SEQ ID NO: 517	HepC1a segment 56	90 nts
SEQ ID NO: 518	Polypeptide encoded by SEQ ID NO: 517	30 aa
SEQ ID NO: 519	HepCla segment 57	90 nts
SEQ ID NO: 520	Polypeptide encoded by SEQ ID NO: 519	30 aa
SEQ ID NO: 521	HepCla segment 58	90 nts
SEQ ID NO: 522	Polypeptide encoded by SEQ ID NO: 521	30 aa
SEQ ID NO: 523	HepCla segment 59	90 nts
SEQ ID NO: 524	Polypeptide encoded by SEQ ID NO: 523	30 aa
SEQ ID NO: 525	HepCla segment 60	90 nts
SEQ ID NO: 526	Polypeptide encoded by SEQ ID NO: 525	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LINGTH
SEQ ID NO: 527	HepCla segment 61	90 nts
SEQ ID NO: 528	Polypeptide encoded by SEQ ID NO: 527	30 aa
SEQ ID NO: 529	HepCla segment 62	90 nts
SEQ ID NO: 530	Polypeptide encoded by SEQ ID NO: 529	30 aa
SEQ ID NO: 531	HepCla segment 63	90 nts
SEQ ID NO: 532	Polypeptide encoded by SEQ ID NO: 531	30 aa
SEQ ID NO: 533	HepCla segment 64	90 nts
SEQ ID NO: 534	Polypeptide encoded by SEQ ID NO: 533	30 aa
SEQ ID NO: 535	HepCla segment 65	90 nts
SEQ ID NO: 536	Polypeptide encoded by SEQ ID NO: 535	30 aa
SEQ ID NO: 537	HepCla segment 66	90 nts
SEQ ID NO: 538	Polypeptide encoded by SEQ ID NO: 537	30 aa
SEQ ID NO: 539	HepCla segment 67	90 nts
SEQ ID NO: 540	Polypeptide encoded by SEQ ID NO: 539	30 aa
SEQ ID NO: 541	HepCla segment 68	90 nts
SEQ ID NO: 542	Polypeptide encoded by SEQ ID NO: 541	30 aa
SEQ ID NO: 543	HepCla segment 69	90 nts
SEQ ID NO: 544	Polypeptide encoded by SEQ ID NO: 543	30 aa
SEQ ID NO: 545	HepCla segment 70	90 nts
SEQ ID NO: 546	Polypeptide encoded by SEQ ID NO:545	30 aa
SEQ ID NO: 547	HepCla segment 71	90 nts
SEQ ID NO: 548	Polypeptide encoded by SEQ ID NO: 547	30 aa
SEQ ID NO: 549	HepCla segment 72	90 nts
SEQ ID NO: 550	Polypeptide encoded by SEQ ID NO: 549	30 aa

SEQUENCE ID NUMBER	NEQUENCE	LENGTH
SEQ ID NO: 551	HepCla segment 73	90 nts
SEQ ID NO: 552	Polypeptide encoded by SEQ ID NO: 551	30 aa
SEQ ID NO: 553	HepCla segment 74	90 nts
SEQ ID NO: 554	Polypeptide encoded by SEQ ID NO: 553	30 aa
SEQ ID NO: 555	HepCla segment 75	90 nts
SEQ ID NO: 556	Polypeptide encoded by SEQ ID NO: 555	30 aa
SEQ ID NO: 557	HepCla segment 76	90 nts
SEQ ID NO: 558	Polypeptide encoded by SEQ ID NO: 557	30 aa
SEQ ID NO: 559	HepCla segment 77	90 nts
SEQ ID NO: 560	Polypeptide encoded by SEQ ID NO: 559	30 aa
SEQ ID NO: 561	HepCla segment 78	90 nts
SEQ ID NO: 562	Polypeptide encoded by SEQ ID NO: 561	30 aa
SEQ ID NO: 563	HepC1a segment 79	90 nts
SEQ ID NO: 564	Polypeptide encoded by SEQ ID NO: 563	30 aa
SEQ ID NO: 565	HepCla segment 80	90 nts
SEQ ID NO: 566	Polypeptide encoded by SEQ ID NO: 565	30 aa
SEQ ID NO: 567	HepCla segment 81	90 nts
SEQ ID NO: 568	Polypeptide encoded by SEQ ID NO: 567	30 aa
SEQ ID NO: 569	HepCla segment 82	90 nts
SEQ ID NO: 570	Polypeptide encoded by SEQ ID NO: 569	30 aa
SEQ ID NO: 571	HepCla segment 83	90 nts
SEQ ID NO: 572	Polypeptide encoded by SEQ ID NO: 571	30 aa
SEQ ID NO: 573	HepCla segment 84	90 nts
SEQ ID NO: 574	Polypeptide encoded by SEQ ID NO: 573	30 aa

SEQUENCE ID NUMBER	SEQUENCS	LENGTH
SEQ ID NO: 575	HepCla segment 85	90 nts
SEQ ID NO: 576	Polypeptide encoded by SEQ ID NO: 575	30 aa
SEQ ID NO: 577	HepCla segment 86	90 nts
SEQ ID NO: 578	Polypeptide encoded by SEQ ID NO: 577	30 aa
SEQ ID NO: 579	HepCla segment 87	90 nts
SEQ ID NO: 580	Polypeptide encoded by SEQ ID NO: 579	30 aa
SEQ ID NO: 581	HepC1a segment 88	90 nts
SEQ ID NO: 582	Polypeptide encoded by SEQ ID NO: 581	30 aa
SEQ ID NO: 583	HepC1a segment 89	90 nts
SEQ ID NO: 584	Polypeptide encoded by SEQ ID NO: 583	30 aa
SEQ ID NO: 585	HepC1a segment 90	90 nts
SEQ ID NO: 586	Polypeptide encoded by SEQ ID NO: 585	30 aa
SEQ ID NO: 587	HepC1a segment 91	90 nts
SEQ ID NO: 588	Polypeptide encoded by SEQ ID NO: 587	30 aa
SEQ ID NO: 589	HepCla segment 92	90 nts
SEQ ID NO: 590	Polypeptide encoded by SEQ ID NO: 589	30 aa
<b>SEQ ID NO: 591</b>	HepCla segment 93	90 nts
<b>SEQ ID NO: 592</b>	Polypeptide encoded by SEQ ID NO: 591	30 aa
<b>SEQ ID NO: 593</b>	HepCla segment 94	90 nts
SEQ ID NO: 594	Polypeptide encoded by SEQ ID NO: 593	30 aa
SEQ ID NO: 595	HepCla segment 95	90 nts
SEQ ID NO: 596	Polypeptide encoded by SEQ ID NO: 595	30 aa
SEQ ID NO: 597	HepCla segment 96	90 nts
SEQ ID NO: 598	Polypeptide encoded by SEQ ID NO: 597	30 aa

SEQUENCE ID NUMBER	SECULNCE	LENGTH
SEQ ID NO: 599	HepCla segment 97	90 nts
SEQ ID NO: 600	Polypeptide encoded by SEQ ID NO: 599	30 aa
SEQ ID NO: 601	HepC1a segment 98	90 nts
SEQ ID NO: 602	Polypeptide encoded by SEQ ID. NO: 601	30 aa
SEQ ID NO: 603	HepCla segment 99	90 nts
SEQ ID NO: 604	Polypeptide encoded by SEQ ID NO: 603	30 aa
SEQ ID NO: 605	HepCla segment 100	90 nts
SEQ ID NO: 606	Polypeptide encoded by SEQ ID NO: 605	30 aa
SEQ ID NO: 607	HepC1a segment 101	90 nts
SEQ ID NO: 608	Polypeptide encoded by SEQ ID NO: 607	30 aa
SEQ ID NO: 609	HepC1a segment 102	90 nts
SEQ ID NO: 610	Polypeptide encoded by SEQ ID NO: 609	30 aa
SEQ ID NO: 611	HepC1a segment 103	90 nts
SEQ ID NO: 612	Polypeptide encoded by SEQ ID NO: 611	30 aa
SEQ ID NO: 613	HepC1a segment 104	90 nts
SEQ ID NO: 614	Polypeptide encoded by SEQ ID NO: 613	30 aa
SEQ ID NO: 615	HepC1a segment 105	90 nts
SEQ ID NO: 616	Polypeptide encoded by SEQ ID NO: 615	30 aa
SEQ ID NO: 617	HepCla segment 106	90 nts
SEQ ID NO: 618	Polypeptide encoded by SEQ ID NO: 617	30 aa
SEQ ID NO: 619	HepCla segment 107	90 nts
<b>SEQ ID NO: 620</b>	Polypeptide encoded by SEQ ID NO: 619	30 aa
SEQ ID NO: 621	HepCla segment 108	90 nts
SEQ ID NO: 622	Polypeptide encoded by SEQ ID NO: 621	30 aa

SEQUENCE II) NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 623	HepCla segment 109	90 nts
SEQ ID NO: 624	Polypeptide encoded by SEQ ID NO: 623	30 aa
SEQ ID NO: 625	HepCla segment 110	90 nts
SEQ ID NO: 626	Polypeptide encoded by SEQ ID NO: 625	30 aa
SEQ ID NO: 627	HepCla segment 111	90 nts
SEQ ID NO: 628	Polypeptide encoded by SEQ ID NO: 627	30 aa
SEQ ID NO: 629	HepC1a segment 112	90 nts
SEQ ID NO: 630	Polypeptide encoded by SEQ ID NO: 629	30 aa
SEQ ID NO: 631	HepCla segment 113	90 nts
SEQ ID NO: 632	Polypeptide encoded by SEQ ID NO: 631	30 aa
SEQ ID NO: 633	HepCla segment 114	90 nts
SEQ ID NO: 634	Polypeptide encoded by SEQ ID NO: 633	30 aa
SEQ ID NO: 635	HepCla segment 115	90 nts
SEQ ID NO: 636	Polypeptide encoded by SEQ ID NO: 635	30 aa
SEQ ID NO: 637	HepCla segment 116	90 nts
SEQ ID NO: 638	Polypeptide encoded by SEQ ID NO: 637	30 aa
SEQ ID NO: 639	HepC1a segment 117	90 nts
SEQ ID NO: 640	Polypeptide encoded by SEQ ID NO: 639	30 aa
SEQ ID NO: 641	HepCla segment 118	90 nts
SEQ ID NO: 642	Polypeptide encoded by SEQ ID NO: 641	30 aa
SEQ ID NO: 643	HepCla segment 119	90 nts
SEQ ID NO: 644	Polypeptide encoded by SEQ ID NO: 643	30 aa
SEQ ID NO: 645	HepC1a segment 120	90 nts
SEQ ID NO: 646	Polypeptide encoded by SEQ ID NO: 645	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 647	HepCla segment 121	90 nts
SEQ ID NO: 648	Polypeptide encoded by SEQ ID NO: 647	30 aa
SEQ ID NO: 649	HepCla segment 122	90 nts
SEQ ID NO: 650	Polypeptide encoded by SEQ ID NO: 649	30 aa
SEQ ID NO: 651	HepCla segment 123	90 nts
SEQ ID NO: 652	Polypeptide encoded by SEQ ID NO: 651	30 aa
SEQ ID NO: 653	HepC1a segment 124	90 nts
SEQ ID NO: 654	Polypeptide encoded by SEQ ID NO: 653	30 aa
SEQ ID NO: 655	HepC1a segment 125	90 nts
SEQ ID NO: 656	Polypeptide encoded by SEQ ID NO: 655	30 aa
SEQ ID NO: 657	HepC1a segment 126	90 nts
SEQ ID NO: 658	Polypeptide encoded by SEQ ID NO: 657	30 aa
SEQ ID NO: 659	HepC1a segment 127	90 nts
SEQ ID NO: 660	Polypeptide encoded by SEQ ID NO: 659	30 aa
SEQ ID NO: 661	HepCla segment 128	90 nts
SEQ ID NO: 662	Polypeptide encoded by SEQ ID NO: 661	30 aa
SEQ ID NO: 663	HepC1a segment 129	90 nts
SEQ ID NO: 664	Polypeptide encoded by SEQ ID NO: 663	30 aa
SEQ ID NO: 665	HepCla segment 130	90 nts
SEQ ID NO: 666	Polypeptide encoded by SEQ ID NO: 665	30 aa
SEQ ID NO: 667	HepCla segment 131	90 nts
SEQ ID NO: 668	Polypeptide encoded by SEQ ID NO: 667	30 aa
SEQ ID NO: 669	HepCla segment 132	90 nts
SEQ ID NO: 670	Polypeptide encoded by SEQ ID NO: 669	30 aa

SEQUENCE ID NUNBER	sequence i	LENGTH
SEQ ID NO: 671	HepCla segment 133	90 nts
SEQ ID NO: 672	Polypeptide encoded by SEQ ID NO: 671	30 aa
SEQ ID NO: 673	HepCla segment 134	90 nts
SEQ ID NO: 674	Polypeptide encoded by SEQ ID NO: 673	30 aa
SEQ ID NO: 675	HepCla segment 135	90 nts
SEQ ID NO: 676	Polypeptide encoded by SEQ ID NO: 675	30 aa
SEQ ID NO: 677	HepCla segment 136	90 nts
SEQ ID NO: 678	Polypeptide encoded by SEQ ID NO: 677	30 aa
SEQ ID NO: 679	HepC1a segment 137	90 nts
SEQ ID NO: 680	Polypeptide encoded by SEQ ID NO: 679	30 aa
SEQ ID NO: 681	HepC1a segment 138	90 nts
SEQ ID NO: 682	Polypeptide encoded by SEQ ID NO: 681	30 aa
SEQ ID NO: 683	HepC1a segment 139	90 nts
SEQ ID NO: 684	Polypeptide encoded by SEQ ID NO: 683	30 aa
SEQ ID NO: 685	HepC1a segment 140	90 nts
SEQ ID NO: 686	Polypeptide encoded by SEQ ID NO: 685	30 aa
SEQ ID NO: 687	HepCla segment 141	90 nts
SEQ ID NO: 688	Polypeptide encoded by SEQ ID NO: 687	30 aa
SEQ ID NO: 689	HepC1a segment 142	90 nts
SEQ ID NO: 690	Polypeptide encoded by SEQ ID NO: 689	30 aa
SEQ ID NO: 691	HepCla segment 143	90 nts
SEQ ID NO: 692	Polypeptide encoded by SEQ ID NO: 691	30 aa
SEQ ID NO: 693	HepCla segment 144	90 nts
SEQ ID NO: 694	Polypeptide encoded by SEQ ID NO: 693	30 aa

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STOUTNCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 695	HepCla segment 145	90 nts
SEQ ID NO: 696	Polypeptide encoded by SEQ ID NO: 695	30 aa
SEQ ID NO: 697	HepCla segment 146	90 nts
SEQ ID NO: 698	Polypeptide encoded by SEQ ID NO: 697	30 aa
SEQ ID NO: 699	HepCla segment 147	90 nts
SEQ ID NO: 700	Polypeptide encoded by SEQ ID NO: 699	30 aa
SEQ ID NO: 701	HepCla segment 148	90 nts
SEQ ID NO: 702	Polypeptide encoded by SEQ ID NO: 701	30 aa
SEQ ID NO: 703	HepCla segment 149	90 nts
SEQ ID NO: 704	Polypeptide encoded by SEQ ID NO: 703	30 aa
SEQ ID NO: 705	HepC1a segment 150	90 nts
SEQ ID NO: 706	Polypeptide encoded by SEQ ID NO: 705	30 aa
SEQ ID NO: 707	HepCla segment 151	90 nts
SEQ ID NO: 708	Polypeptide encoded by SEQ ID NO: 707	30 aa
SEQ ID NO: 709	HepCla segment 152	90 nts
SEQ ID NO: 710	Polypeptide encoded by SEQ ID NO: 709	30 aa
SEQ ID NO: 711	HepCla segment 153	90 nts
SEQ ID NO: 712	Polypeptide encoded by SEQ ID NO: 711	30 aa
SEQ ID NO: 713	HepCla segment 154	90 nts
SEQ ID NO: 714	Polypeptide encoded by SEQ ID NO: 713	30 aa
SEQ ID NO: 715	HepC1a segment 155	90 nts
SEQ ID NO: 716	Polypeptide encoded by SEQ ID NO: 715	30 aa
SEQ ID NO: 717	HepCla segment 156	90 nts
SEQ ID NO: 718	Polypeptide encoded by SEQ ID NO: 717	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LINGTH
SEQ ID NO: 719	HepCla segment 157	90 nts
SEQ ID NO: 720	Polypeptide encoded by SEQ ID NO: 719	30 aa
SEQ ID NO: 721	HepCla segment 158	90 nts
SEQ ID NO: 722	Polypeptide encoded by SEQ ID NO: 721	30 aa
SEQ ID NO: 723	HepC1a segment 159	90 nts
SEQ ID NO: 724	Polypeptide encoded by SEQ ID NO: 723	30 aa
SEQ ID NO: 725	HepCla segment 160	90 nts
SEQ ID NO: 726	Polypeptide encoded by SEQ ID NO: 725	30 aa
SEQ ID NO: 727	HepC1a segment 161	90 nts
SEQ ID NO: 728	Polypeptide encoded by SEQ ID NO: 727	30 aa
SEQ ID NO: 729	HepCla segment 162	90 nts
SEQ ID NO: 730	Polypeptide encoded by SEQ ID NO: 729	30 aa
SEQ ID NO: 731	HepC1a segment 163	90 nts
SEQ ID NO: 732	Polypeptide encoded by SEQ ID NO: 731	30 aa
SEQ ID NO: 733	HepCla segment 164	90 nts
<b>SEQ ID NO: 734</b>	Polypeptide encoded by SEQ ID NO: 733	30 aa
SEQ ID NO: 735	HepC1a segment 165	90 nts
SEQ ID NO: 736	Polypeptide encoded by SEQ ID NO: 735	30 aa
<b>SEQ ID NO: 737</b>	HepCla segment 166	90 nts
<b>SEQ ID NO: 738</b>	Polypeptide encoded by SEQ ID NO: 737	30 aa
SEQ ID NO: 739	HepCla segment 167	90 nts
SEQ ID NO: 740	Polypeptide encoded by SEQ ID NO: 739	30 aa
SEQ ID NO: 741	HepCla segment 168	90 nts
SEQ ID NO: 742	Polypeptide encoded by SEQ ID NO: 741	30 aa

SIQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 743	HepCla segment 169	90 nts
SEQ ID NO: 744	Polypeptide encoded by SEQ ID NO: 743	30 aa
SEQ ID NO: 745	HepCla segment 170	90 nts
SEQ ID NO: 746	Polypeptide encoded by SEQ ID NO: 745	30 aa
SEQ ID NO: 747	HepCla segment 171	90 nts
SEQ ID NO: 748	Polypeptide encoded by SEQ ID NO: 747	30 aa
SEQ ID NO: 749	HepC1a segment 172	90 nts
SEQ ID NO: 750	Polypeptide encoded by SEQ ID NO: 749	30 aa
SEQ ID NO: 751	HepCla segment 173	90 nts
SEQ ID NO: 752	Polypeptide encoded by SEQ ID NO: 751	30 aa
SEQ ID NO: 753	HepCla segment 174	90 nts
SEQ ID NO: 754	Polypeptide encoded by SEQ ID NO: 753	30 aa
SEQ ID NO: 755	HepCla segment 175	90 nts
SEQ ID NO: 756	Polypeptide encoded by SEQ ID NO: 755	30 aa
SEQ ID NO: 757	HepCla segment 176	90 nts
SEQ ID NO: 758	Polypeptide encoded by SEQ ID NO: 757	30 aa
SEQ ID NO: 759	HepCla segment 177	90 nts
SEQ ID NO: 760	Polypeptide encoded by SEQ ID NO: 759	30 aa
SEQ ID NO: 761	HepCla segment 178	90 nts
SEQ ID NO: 762	Polypeptide encoded by SEQ ID NO: 761	30 aa
SEQ ID NO: 763	HepCla segment 179	90 nts
SEQ ID NO: 764	Polypeptide encoded by SEQ ID NO: 763	30 aa
SEQ ID NO: 765	HepCla segment 180	90 nts
SEQ ID NO: 766	Polypeptide encoded by SEQ ID NO: 765	30 aa

SEQUENCE ID	<u>SEOUENCE</u>	i Pinciru
NUMBER		LENGTH
SEQ ID NO: 767	HepCla segment 181	90 nts
SEQ ID NO: 768	Polypeptide encoded by SEQ ID NO: 767	30 aa
SEQ ID NO: 769	HepCla segment 182	90 nts
SEQ ID NO: 770	Polypeptide encoded by SEQ ID NO: 769	30 aa
SEQ ID NO: 771	HepCla segment 183	90 nts
SEQ ID NO: 772	Polypeptide encoded by SEQ ID NO: 771	·30 aa
SEQ ID NO: 773	HepCla segment 184	90 nts
SEQ ID NO: 774	Polypeptide encoded by SEQ ID NO: 773	30 aa
SEQ ID NO: 775	HepCla segment 185	90 nts
SEQ ID NO: 776	Polypeptide encoded by SEQ ID NO: 775	30 aa
SEQ ID NO: 777	HepCla segment 186	90 nts
SEQ ID NO: 778	Polypeptide encoded by SEQ ID NO: 777	30 aa
SEQ ID NO: 779	HepC1a segment 187	90 nts
SEQ ID NO: 780	Polypeptide encoded by SEQ ID NO: 779	30 aa
SEQ ID NO: 781	HepCla segment 188	90 nts
SEQ ID NO: 782	Polypeptide encoded by SEQ ID NO: 781	30 aa
SEQ ID NO: 783	HepCla segment 189	90 nts
<b>SEQ ID NO: 784</b>	Polypeptide encoded by SEQ ID NO: 783	30 aa
SEQ ID NO: 785	HepCla segment 190	90 nts
SEQ ID NO: 786	Polypeptide encoded by SEQ ID NO: 785	30 aa
SEQ ID NO: 787	HepCla segment 191	90 nts
SEQ ID NO: 788	Polypeptide encoded by SEQ ID NO: 787	30 aa
SEQ ID NO: 789	HepCla segment 192	90 nts
SEQ ID NO: 790	Polypeptide encoded by SEQ ID NO: 789	30 aa

SEQUENCS ID MUMBER	SEQUENCE	LENGTH
SEQ ID NO: 791	HepCla segment 193	90 nts
SEQ ID NO: 792	Polypeptide encoded by SEQ ID NO: 791	30 aa
SEQ ID NO: 793	HepCla segment 194	90 nts
SEQ ID NO: 794	Polypeptide encoded by SEQ ID NO: 793	30 aa
SEQ ID NO: 795	HepC1a segment 195	90 nts
SEQ ID NO: 796	Polypeptide encoded by SEQ ID NO: 795	30 aa
SEQ ID NO: 797	HepCla segment 196	90 nts
SEQ ID NO: 798	Polypeptide encoded by SEQ ID NO: 797	30 aa
SEQ ID NO: 799	HepC1a segment 197	90 nts
SEQ ID NO: 800	Polypeptide encoded by SEQ ID NO: 799	30 aa
SEQ ID NO: 801	HepC1a segment 198	9θ nts
SEQ ID NO: 802	Polypeptide encoded by SEQ ID NO: 801	30 aa
SEQ ID NO: 803	HepCla segment 199	90 nts
SEQ ID NO: 804	Polypeptide encoded by SEQ ID NO: 803	30 aa
SEQ ID NO: 805	HepC1a segment 200	90 nts
SEQ ID NO: 806	Polypeptide encoded by SEQ ID NO: 805	30 aa
SEQ ID NO: 807	HepC1a segment 201	45 nts
SEQ ID NO: 808	Polypeptide encoded by SEQ ID NO: 807	15 aa
SEQ ID NO: 809	HepCla scrambled	17955 nts
SEQ ID NO: 810	Polypeptide encoded by SEQ ID NO: 809	5985 aa
SEQ ID NO: 811	HepC Cassette A	6065 nts
SEQ ID NO: 812	Polypeptide encoded by SEQ ID NO: 811	2011 aa
SEQ ID NO: 813	HepC Cassette B	6069 nts
SEQ ID NO: 814	Polypeptide encoded by SEQ ID NO: 813	2010 aa

SEQUENCE ID NUMBUR	SEQUENCE	LENGTH
SEQ ID NO: 815	HepC Cassette C	6030 nts
SEQ ID NO: 816	Polypeptide encoded by SEQ ID NO: 815	1997 aa
SEQ ID NO: 817	gp100 consensus polypeptide	661 aa
SEQ ID NO: 818	MART consensus polypeptide	118 aa
SEQ ID NO: 819	TRP-1 consensus polypeptide	248 aa
SEQ ID NO: 820	Tyros consensus polypeptide	529 aa
SEQ ID NO: 821	TRP2 consensus polypeptide	519 aa
SEQ ID NO: 822	MC1R consensus polypeptide	317 aa
SEQ ID NO: 823	MUC1F consensus polypeptide	125 aa
SEQ ID NO: 824	MUC1R consensus polypeptide	312 aa
SEQ ID NO: 825	BAGE consensus polypeptide	43 aa
SEQ ID NO: 826	GAGE-1 consensus polypeptide	138 aa
SEQ ID NO: 827	gp100ln4 consensus polypeptide	51 aa
SEQ ID NO: 828	MAGE-1 consensus polypeptide	309 aa
SEQ ID NO: 829	MAGE-3 consensus polypeptide	314 aa
SEQ ID NO: 830	PRAME consensus polypeptide	509 aa
SEQ ID NO: 831	TRP2IN2 consensus polypeptide	54 aa
SEQ ID NO: 832	NYNSO1a consensus polypeptide	180 aa
SEQ ID NO: 833	NYNSO1b consensus polypeptide	58 aa
SEQ ID NO: 834	LAGE1 consensus polypeptide	180 aa
SEQ ID NO: 835	gp100 segment 1	90 nts
SEQ ID NO: 836	Polypeptide encoded by SEQ ID NO: 835	30 aa
SEQ ID NO: 837	gp100 segment 2	90 nts
SEQ ID NO: 838	Polypeptide encoded by SEQ ID NO: 837	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENCTH
SEQ ID NO: 839	gp100 segment 3	90 nts
SEQ ID NO: 840	Polypeptide encoded by SEQ ID NO: 839	30 aa
SEQ ID NO: 841	gp100 segment 4	90 nts
SEQ ID NO: 842	Polypeptide encoded by SEQ ID NO: 841	30 aa
SEQ ID NO: 843	gp100 segment 5	90 nts
SEQ ID NO: 844	Polypeptide encoded by SEQ ID NO: 843	30 aa
SEQ ID NO: 845	gp100 segment 6	90 nts
SEQ ID NO: 846	Polypeptide encoded by SEQ ID NO: 845	30 aa ,
SEQ ID NO: 847	gp100 segment 7	90 nts
SEQ ID NO: 848	Polypeptide encoded by SEQ ID NO: 847	30 aa
SEQ ID NO: 849	gp100 segment 8	90 nts
SEQ ID NO: 850	Polypeptide encoded by SEQ ID NO: 849	30 aa
SEQ ID NO: 851	gp100 segment 9	90 nts
SEQ ID NO: 852	Polypeptide encoded by SEQ ID NO: 851	30 aa
SEQ ID NO: 853	gp100 segment 10	90 nts
SEQ ID NO: 854	Polypeptide encoded by SEQ ID NO: 853	30 aa
SEQ ID NO: 855	gp100 segment 11	90 nts
SEQ ID NO: 856	Polypeptide encoded by SEQ ID NO: 855	30 aa
SEQ ID NO: 857	gp100 segment 12	90 nts
SEQ ID NO: 858	Polypeptide encoded by SEQ ID NO: 857	30 aa
SEQ ID NO: 859	gp100 segment 13	90 nts
SEQ ID NO: 860	Polypeptide encoded by SEQ ID NO: 859	30 aa
SEQ ID NO: 861	gp100 segment 14	90 nts
SEQ ID NO: 862	Polypeptide encoded by SEQ ID NO: 861	30 aa

SEQUENCE ID NUMBER	SECHENCE	LENGTH
SEQ ID NO: 863	gp100 segment 15	90 nts
SEQ ID NO: 864	Polypeptide encoded by SEQ ID NO: 863	30 aa
SEQ ID NO: 865	gp100 segment 16	90 nts
SEQ ID NO: 866	Polypeptide encoded by SEQ ID NO: 865	30 aa
SEQ ID NO: 867	gp100 segment 17	90 nts
SEQ ID NO: 868	Polypeptide encoded by SEQ ID NO: 867	30 aa
SEQ ID NO: 869	gp100 segment 18	90 nts
SEQ ID NO: 870	Polypeptide encoded by SEQ ID NO: 869	30 aa
SEQ ID NO: 871	gp100 segment 19	90 nts
SEQ ID NO: 872	Polypeptide encoded by SEQ ID NO: 871	30 aa
SEQ ID NO: 873	gp100 segment 20	90 nts
SEQ ID NO: 874	Polypeptide encoded by SEQ ID NO: 873	30 aa
SEQ ID NO: 875	gp100 segment 21	90 nts
SEQ ID NO: 876	Polypeptide encoded by SEQ ID NO: 875	30 aa
SEQ ID NO: 877	gp100 segment 22	90 nts
SEQ ID NO: 878	Polypeptide encoded by SEQ ID NO: 877	30 aa
SEQ ID NO: 879	gp100 segment 23	90 nts
SEQ ID NO: 880	Polypeptide encoded by SEQ ID NO: 879	30 aa
SEQ ID NO: 881	gp100 segment 24	90 nts
SEQ ID NO: 882	Polypeptide encoded by SEQ ID NO: 881	30 aa
SEQ ID NO: 883	gp100 segment 25	90 nts
SEQ ID NO: 884	Polypeptide encoded by SEQ ID NO: 883	30 aa
SEQ ID NO: 885	gp100 segment 26	90 nts
SEQ ID NO: 886	Polypeptide encoded by SEQ ID NO: 885	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LIENGTH
SEQ ID NO: 887	gp100 segment 27	90 nts
SEQ ID NO: 888	Polypeptide encoded by SEQ ID NO: 887	30 aa
SEQ ID NO: 889	gp100 segment 28	90 nts
SEQ ID NO: 890	Polypeptide encoded by SEQ ID NO: 889	30 aa
SEQ ID NO: 891	gp100 segment 29	90 nts
SEQ ID NO: 892	Polypeptide encoded by SEQ ID NO: 891	30 aa
SEQ ID NO: 893	gp100 segment 30	90 nts
SEQ ID NO: 894	Polypeptide encoded by SEQ ID NO: 893	30 aa
SEQ ID NO: 895	gp100 segment 31	90 nts
SEQ ID NO: 896	Polypeptide encoded by SEQ ID NO: 895	30 aa
SEQ ID NO: 897	gp100 segment 32	90 nts
SEQ ID NO: 898	Polypeptide encoded by SEQ ID NO: 897	30 aa
SEQ ID NO: 899	gp100 segment 33	90 nts
SEQ ID NO: 900	Polypeptide encoded by SEQ ID NO: 899	30 aa
SEQ ID NO: 901	gp100 segment 34	90 nts
SEQ ID NO: 902	Polypeptide encoded by SEQ ID NO: 901	30 aa
SEQ ID NO: 903	gp100 segment 35	90 nts
SEQ ID NO: 904	Polypeptide encoded by SEQ ID NO: 903	30 aa
SEQ ID NO: 905	gp100 segment 36	90 nts
SEQ ID NO: 906	Polypeptide encoded by SEQ ID NO: 905	30 aa
SEQ ID NO: 907	gp100 segment 37	90 nts
SEQ ID NO: 908	Polypeptide encoded by SEQ ID NO: 907	30 aa
SEQ ID NO: 909	gp100 segment 38	90 nts
SEQ ID NO: 910	Polypeptide encoded by SEQ ID NO: 909	30 aa

STQUENCE ID NUMBER	: Siguence	LINGTH
SEQ ID NO: 911	gp100 segment 39	90 nts
SEQ ID NO: 912	Polypeptide encoded by SEQ ID NO: 911	30 aa
SEQ ID NO: 913	gp100 segment 40	90 nts
SEQ ID NO: 914	Polypeptide encoded by SEQ ID NO: 913	30 aa
SEQ ID NO: 915	gp100 segment 41	90 nts
SEQ ID NO: 916	Polypeptide encoded by SEQ ID NO: 915	30 aa
SEQ ID NO: 917	gp100 segment 42	90 nts
SEQ ID NO: 918	Polypeptide encoded by SEQ ID NO: 917	30 aa
SEQ ID NO: 919	gp100 segment 43	90 nts
SEQ ID NO: 920	Polypeptide encoded by SEQ ID NO: 919	30 aa
SEQ ID NO: 921	gp100 segment 44	60nts
SEQ ID NO: 922	Polypeptide encoded by SEQ ID NO: 921	20 aa
SEQ ID NO: 923	MART segment 1	90 nts
SEQ ID NO: 924	Polypeptide encoded by SEQ ID NO: 923	30 aa
SEQ ID NO: 925	MART segment 2	90 nts
SEQ ID NO: 926	Polypeptide encoded by SEQ ID NO: 925	30 aa
SEQ ID NO: 927	MART segment 3	90 nts
SEQ ID NO: 928	Polypeptide encoded by SEQ ID NO: 927	30 aa
SEQ ID NO: 929	MART segment 4	90 nts
SEQ ID NO: 930	Polypeptide encoded by SEQ ID NO: 929	30 aa
SEQ ID NO: 931	MART segment 5	90 nts
SEQ ID NO: 932	Polypeptide encoded by SEQ ID NO: 931	30 aa
SEQ ID NO: 933	MART segment 6	90 nts
SEQ ID NO: 934	Polypeptide encoded by SEQ ID NO: 933	30 aa

SEQUENCE ID NUMBER	SEQUÊNCE.	LENGTH
SEQ ID NO: 935	MART segment 7	90 nts
SEQ ID NO: 936	Polypeptide encoded by SEQ ID NO: 935	30 aa
SEQ ID NO: 937	MART segment 8	51 nts
SEQ ID NO: 938	Polypeptide encoded by SEQ ID NO: 937	17 aa
SEQ ID NO: 939	trp-1 segment 1	90 nts
SEQ ID NO: 940	Polypeptide encoded by SEQ ID NO: 939	30 aa
SEQ ID NO: 941	trp-1 segment 2	90 nts
SEQ ID NO: 942	Polypeptide encoded by SEQ ID NO: 941	30 aa
SEQ ID NO: 943	trp-1 segment 3	90 nts
SEQ ID NO: 944	Polypeptide encoded by SEQ ID NO: 943	30 aa
SEQ ID NO: 945	trp-1 segment 4	90 nts
SEQ ID NO: 946	Polypeptide encoded by SEQ ID NO: 945	30 aa
SEQ ID NO: 947	trp-1 segment 5	90 nts
SEQ ID NO: 948	Polypeptide encoded by SEQ ID NO: 947	30 aa
SEQ ID NO: 949	trp-1 segment 6	90 nts
SEQ ID NO: 950	Polypeptide encoded by SEQ ID NO: 949	30 aa
SEQ ID NO: 951	trp-1 segment 7	90 nts
SEQ ID NO: 952	Polypeptide encoded by SEQ ID NO: 951	30 aa
SEQ ID NO: 953	trp-1 segment 8	90 nts
<b>SEQ ID NO: 954</b>	Polypeptide encoded by SEQ ID NO: 953	30 aa
<b>SEQ ID NO: 955</b>	trp-1 segment 9	90 nts
<b>SEQ ID NO: 956</b>	Polypeptide encoded by SEQ ID NO: 955	30 aa
SEQ ID NO: 957	trp-1 segment 10	90 nts
SEQ ID NO: 958	Polypeptide encoded by SEQ ID NO: 957	30 aa

SIQUENCI ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 959	trp-1 segment 11	90 nts
SEQ ID NO: 960	Polypeptide encoded by SEQ ID NO: 959	30 aa
SEQ ID NO: 961	trp-1 segment 12	90 nts
SEQ ID NO: 962	Polypeptide encoded by SEQ ID NO: 961	30 aa
SEQ ID NO: 963	trp-1 segment 13	90 nts
SEQ ID NO: 964	Polypeptide encoded by SEQ ID NO: 963	30 aa
SEQ ID NO: 965	trp-1 segment 14	90 nts
SEQ ID NO: 966	Polypeptide encoded by SEQ ID NO: 965	30 aa
SEQ ID NO: 967	trp-1 segment 15	90 nts
SEQ ID NO: 968	Polypeptide encoded by SEQ ID NO: 967	30 aa
SEQ ID NO: 969	trp-1 segment 16	81 nts
SEQ ID NO: 970	Polypeptide encoded by SEQ ID NO: 969	27 aa
SEQ ID NO: 971	tyros segment 1	90 nts
SEQ ID NO: 972	Polypeptide encoded by SEQ ID NO: 971	30 aa
<b>SEQ ID NO: 973</b>	tyros segment 2	90 nts
SEQ ID NO: 974	Polypeptide encoded by SEQ ID NO: 973	30 aa
<b>SEQ ID NO: 975</b>	tyros segment 3	90 nts
<b>SEQ ID NO: 976</b>	Polypeptide encoded by SEQ ID NO: 975	30 aa
<b>SEQ ID NO: 977</b>	tyros segment 4	90 nts
SEQ ID NO: 978	Polypeptide encoded by SEQ ID NO: 977	30 aa
SEQ ID NO: 979	tyros segment 5	90 nts
SEQ ID NO: 980	Polypeptide encoded by SEQ ID NO: 979	30 aa
SEQ ID NO: 981	tyros segment 6	90 nts
SEQ ID NO: 982	Polypeptide encoded by SEQ ID NO: 981	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 983	tyros segment 7	90 nts
SEQ ID NO: 984	Polypeptide encoded by SEQ ID NO: 983	30 aa
SEQ ID NO: 985	tyros segment 8	90 nts
SEQ ID NO: 986	Polypeptide encoded by SEQ ID NO: 985	30 aa
SEQ ID NO: 987	tyros segment 9	90 nts
SEQ ID NO: 988	Polypeptide encoded by SEQ ID NO: 987	30 aa
SEQ ID NO: 989	tyros segment 10	90 nts
SEQ ID NO: 990	Polypeptide encoded by SEQ ID NO: 989	30 aa
SEQ ID NO: 991	tyros segment 11	90 nts
SEQ ID NO: 992	Polypeptide encoded by SEQ ID NO: 991	30 aa
SEQ ID NO: 993	tyros segment 12	90 nts
SEQ ID NO: 994	Polypeptide encoded by SEQ ID NO: 993	30 aa
SEQ ID NO: 995	tyros segment 13	90 nts
SEQ ID NO: 996	Polypeptide encoded by SEQ ID NO: 995	30 aa
SEQ ID NO: 997	tyros segment 14	90 nts
SEQ ID NO: 998	Polypeptide encoded by SEQ ID NO: 997	30 aa
SEQ ID NO: 999	tyros segment 15	90 nts
SEQ ID NO: 1000	Polypeptide encoded by SEQ ID NO: 999	30 aa
SEQ ID NO: 1001	tyros segment 16	90 nts
SEQ ID NO: 1002	Polypeptide encoded by SEQ ID NO: 1001	30 aa
SEQ ID NO: 1003	tyros segment 17	90 nts
SEQ ID NO: 1004	Polypeptide encoded by SEQ ID NO: 1003	30 aa
SEQ ID NO: 1005	tyros segment 18	90 nts
<b>SEQ ID NO: 1006</b>	Polypeptide encoded by SEQ ID NO: 1005	30 aa

SEQUENCE ID AUMBER	SEQUENCE	UINGTH
SEQ ID NO: 1007	tyros segment 19	90 nts
SEQ ID NO: 1008	Polypeptide encoded by SEQ ID NO: 1007	30 aa
SEQ ID NO: 1009	tyros segment 20	90 nts
SEQ ID NO: 1010	Polypeptide encoded by SEQ ID NO: 1009	30 aa
SEQ ID NO: 1011	tyros segment 21	90 nts
SEQ ID NO: 1012	Polypeptide encoded by SEQ ID NO: 1011	30 aa
SEQ ID NO: 1013	tyros segment 22	90 nts
SEQ ID NO: 1014	Polypeptide encoded by SEQ ID NO: 1013	30 aa
SEQ ID NO: 1015	tyros segment 23	90 nts
SEQ ID NO: 1016	Polypeptide encoded by SEQ ID NO: 1015	30 aa
SEQ ID NO: 1017	tyros segment 24	90 nts
SEQ ID NO: 1018	Polypeptide encoded by SEQ ID NO: 1017	30 aa
SEQ ID NO: 1019	tyros segment 25	90 nts
SEQ ID NO: 1020	Polypeptide encoded by SEQ ID NO: 1019	30 aa
SEQ ID NO: 1021	tyros segment 26	90 nts
SEQ ID NO: 1022	Polypeptide encoded by SEQ ID NO: 1021	30 aa
SEQ ID NO: 1023	tyros segment 27	90 nts
SEQ ID NO: 1024	Polypeptide encoded by SEQ ID NO: 1023	30 aa
SEQ ID NO: 1025	tyros segment 28	90 nts
SEQ ID NO: 1026	Polypeptide encoded by SEQ ID NO: 1025	30 aa
SEQ ID NO: 1027	tyros segment 29	90 nts
SEQ ID NO: 1028	Polypeptide encoded by SEQ ID NO: 1027	30 aa
SEQ ID NO: 1029	tyros segment 30	90 nts
SEQ ID NO: 1030	Polypeptide encoded by SEQ ID NO: 1029	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1031	tyros segment 31	90 nts
SEQ ID NO: 1032	Polypeptide encoded by SEQ ID NO: 1031	30 aa
SEQ ID NO: 1033	tyros segment 32	90 nts
SEQ ID NO: 1034	Polypeptide encoded by SEQ ID NO: 1033	30 aa
SEQ ID NO: 1035	tyros segment 33	90 nts
SEQ ID NO: 1036	Polypeptide encoded by SEQ ID NO: 1035	30 aa
SEQ ID NO: 1037	tyros segment 34	90 nts
SEQ ID NO: 1038	Polypeptide encoded by SEQ ID NO: 1037	30 aa
SEQ ID NO: 1039	tyros segment 35	69 nts
SEQ ID NO: 1040	Polypeptide encoded by SEQ ID NO: 1039	23 aa
SEQ ID NO: 1041	trp2 segment 1	90 nts
SEQ ID NO: 1042	Polypeptide encoded by SEQ ID NO: 1041	30 aa
SEQ ID NO: 1043.	trp2 segment 2	90 nts
SEQ ID NO: 1044	Polypeptide encoded by SEQ ID NO: 1043	30 aa
SEQ ID NO: 1045	trp2 segment 3	90 nts
SEQ ID NO: 1046	Polypeptide encoded by SEQ ID NO: 1045	30 aa
SEQ ID NO: 1047	trp2 segment 4	90 nts
SEQ ID NO: 1048	Polypeptide encoded by SEQ ID NO: 1047	30 aa
SEQ ID NO: 1049	trp2 segment 5	90 nts
SEQ ID NO: 1050	Polypeptide encoded by SEQ ID NO: 1049	30 aa
SEQ ID NO: 1051	trp2 segment 6	90 nts
SEQ ID NO: 1052	Polypeptide encoded by SEQ ID NO: 1051	30 aa
SEQ ID NO: 1053	trp2.segment 7	90 nts
SEQ ID NO: 1054	Polypeptide encoded by SEQ ID NO: 1053	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1055	trp2 segment 8	90 nts
SEQ ID NO: 1056	Polypeptide encoded by SEQ ID NO: 1055	30 aa
SEQ ID NO: 1057	trp2 segment 9	90 nts
SEQ ID NO: 1058	Polypeptide encoded by SEQ ID NO: 1057	30 aa
SEQ ID NO: 1059	trp2 segment 10	90 nts
SEQ ID NO: 1060	Polypeptide encoded by SEQ ID NO: 1059	30 aa
SEQ ID NO: 1061	trp2 segment 11	90 nts
SEQ ID NO: 1062	Polypeptide encoded by SEQ ID NO: 1061	30 aa
SEQ ID NO: 1063	trp2 segment 12	90 nts
SEQ ID NO: 1064	Polypeptide encoded by SEQ ID NO: 1063	30 aa
SEQ ID NO: 1065	trp2 segment 13	90 nts
SEQ ID NO: 1066	Polypeptide encoded by SEQ ID NO: 1065	30 aa
SEQ ID NO: 1067	trp2 segment 14	90 nts
SEQ ID NO: 1068	Polypeptide encoded by SEQ ID NO: 1067	30 aa
SEQ ID NO: 1069	trp2 segment 15	90 nts
SEQ ID NO: 1070	Polypeptide encoded by SEQ ID NO: 1069	30 aa
SEQ ID NO: 1071	trp2 segment 16	90 nts
SEQ ID NO: 1072	Polypeptide encoded by SEQ ID NO: 1071	30 aa
SEQ ID NO: 1073	trp2 segment 17	90 nts
SEQ ID NO: 1074	Polypeptide encoded by SEQ ID NO: 1073	30 aa
SEQ ID NO: 1075	trp2 segment 18	90 nts
SEQ ID NO: 1076	Polypeptide encoded by SEQ ID NO: 1075	30 aa
SEQ ID NO: 1077	trp2 segment 19	90 nts
SEQ ID NO: 1078	Polypeptide encoded by SEQ ID NO: 1077	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1079	trp2 segment 20	90 nts
SEQ ID NO: 1080	Polypeptide encoded by SEQ ID NO: 1079	30 aa 、
SEQ ID NO: 1081	trp2 segment 21	90 nts
SEQ ID NO: 1082	Polypeptide encoded by SEQ ID NO: 1081	30 aa
SEQ ID NO: 1083	trp2 segment 22	90 nts
SEQ ID NO: 1084	Polypeptide encoded by SEQ ID NO: 1083	30 aa
SEQ ID NO: 1085	trp2 segment 23	90 nts
SEQ ID NO: 1086	Polypeptide encoded by SEQ ID NO: 1085	30 aa
SEQ ID NO: 1087	trp2 segment 24	90 nts
SEQ ID NO: 1088	Polypeptide encoded by SEQ ID NO: 1087	30 aa
SEQ ID NO: 1089	trp2 segment 25	90 nts
SEQ ID NO: 1090	Polypeptide encoded by SEQ ID NO: 1089	30 aa
SEQ ID NO: 1091	trp2 segment 26	90 nts
SEQ ID NO: 1092	Polypeptide encoded by SEQ ID NO: 1091	30 aa
SEQ ID NO: 1093	trp2 segment 27	90 nts
SEQ ID NO: 1094	Polypeptide encoded by SEQ ID NO: 1093	30 aa
SEQ ID NO: 1095	trp2 segment 28	90 nts
SEQ ID NO: 1096	Polypeptide encoded by SEQ ID NO: 1095	30 aa
SEQ ID NO: 1097	trp2 segment 29	90 nts
SEQ ID NO: 1098	Polypeptide encoded by SEQ ID NO: 1097	30 aa
SEQ ID NO: 1099	trp2 segment 30	90 nts
SEQ ID NO: 1100	Polypeptide encoded by SEQ ID NO: 1099	30 aa
SEQ ID NO: 1101	trp2 segment 31	90 nts
SEQ ID NO: 1102	Polypeptide encoded by SEQ ID NO: 1101	30 aa

SEQUENCE ID NUMBER	SEQUENCS	LENGTH
SEQ ID NO: 1103	trp2 segment 32	90 nts
SEQ ID NO: 1104	Polypeptide encoded by SEQ ID NO: 1103	30 aa
SEQ ID NO: 1105	trp2 segment 33	90 nts
SEQ ID NO: 1106	Polypeptide encoded by SEQ ID NO: 1105	30 aa
SEQ ID NO: 1107	trp2 segment 34	84 nts
SEQ ID NO: 1108	Polypeptide encoded by SEQ ID NO: 1107	28 aa
SEQ ID NO: 1109	MC1R segment 1	90 nts
SEQ ID NO: 1110	Polypeptide encoded by SEQ ID NO: 1109	30 aa
SEQ ID NO: 1111	MC1R segment 2	90 nts
SEQ ID NO: 1112	Polypeptide encoded by SEQ ID NO: 1111	30 aa
SEQ ID NO: 1113	MC1R segment 3	90 nts
SEQ ID NO: 1114	Polypeptide encoded by SEQ ID NO: 1113	30 aa
SEQ ID NO: 1115	MC1R segment 4	90 nts
SEQ ID NO: 1116	Polypeptide encoded by SEQ ID NO: 1115	30 aa
SEQ ID NO: 1117	MC1R segment 5	90 nts
SEQ ID NO: 1118	Polypeptide encoded by SEQ ID NO: 1117	30 aa
SEQ ID NO: 1119	MC1R segment 6	90 nts
SEQ ID NO: 1120	Polypeptide encoded by SEQ ID NO: 1119	30 aa
SEQ ID NO: 1121	MC1R segment 7	90 nts
SEQ ID NO: 1122	Polypeptide encoded by SEQ ID NO: 1121	30 aa
SEQ ID NO: 1123	MC1R segment 8	90 nts
SEQ ID NO: 1124	Polypeptide encoded by SEQ ID NO: 1123	30 aa
SEQ ID NO: 1125	MC1R segment 9	90 nts
SEQ ID NO: 1126	Polypeptide encoded by SEQ ID NO: 1125	30 aa

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SEQUENCE ID NUMBER	SEQUENCE L	LENGTH
SEQ ID NO: 1127	MC1R segment 10	90 nts
SEQ ID NO: 1128	Polypeptide encoded by SEQ ID NO: 1127	30 aa
SEQ ID NO: 1129	MC1R segment 11	90 nts
SEQ ID NO: 1130	Polypeptide encoded by SEQ ID NO: 1129	30 aa
SEQ ID NO: 1131	MC1R segment 12	90 nts
SEQ ID NO: 1132	Polypeptide encoded by SEQ ID NO: 1131	30 aa
SEQ ID NO: 1133	MC1R segment 13	90 nts
SEQ ID NO: 1134	Polypeptide encoded by SEQ ID NO: 1133	30 aa
SEQ ID NO: 1135	MC1R segment 14	90 nts
SEQ ID NO: 1136	Polypeptide encoded by SEQ ID NO: 1135	30 aa
SEQ ID NO: 1137	MC1R segment 15	90 nts
SEQ ID NO: 1138	Polypeptide encoded by SEQ ID NO: 1137	30 aa
SEQ ID NO: 1139	MC1R segment 16	90 nts
SEQ ID NO: 1140	Polypeptide encoded by SEQ ID NO: 1139	30 aa
SEQ ID NO: 1141	MC1R segment 17	90 nts
<b>SEQ ID NO: 1142</b>	Polypeptide encoded by SEQ ID NO: 1141	30 aa
SEQ ID NO: 1143	MC1R segment 18	90 nts
SEQ ID NO: 1144	Polypeptide encoded by SEQ ID NO: 1143	30 aa
SEQ ID NO: 1145	MC1R segment 19	90 nts
SEQ ID NO: 1146	Polypeptide encoded by SEQ ID NO: 1145	30 aa
SEQ ID NO: 1147	MC1R segment 20	90 nts
SEQ ID NO: 1148	Polypeptide encoded by SEQ ID NO: 1147	30 aa
SEQ ID NO: 1149	MC1R segment 21	63 nts
SEQ ID NO: 1150	Polypeptide encoded by SEQ ID NO: 1149	21 aa

SIQUENCI ID NUMBIR	SEQUENCE	LENGTH
SEQ ID NO: 1151	MUC1F segment 1	90 nts
SEQ ID NO: 1152	Polypeptide encoded by SEQ ID NO: 1151	30 aa
SEQ ID NO: 1153	MUC1F segment 2	90 nts
SEQ ID NO: 1154	Polypeptide encoded by SEQ ID NO: 1153	30 aa
SEQ ID NO: 1155	MUC1F segment 3	90 nts
SEQ ID NO: 1156		
SEQ ID NO: 1157	Polypeptide encoded by SEQ ID NO: 1155	30 aa
SEQ ID NO: 1158	MUC1F segment 4	90 nts
`	Polypeptide encoded by SEQ ID NO: 1157	30 aa
SEQ ID NO: 1159	MUC1F segment 5	90 nts
SEQ ID NO: 1160	Polypeptide encoded by SEQ ID NO: 1159	30 aa
SEQ ID NO: 1161	MUC1F segment 6	90 nts
SEQ ID NO: 1162	Polypeptide encoded by SEQ ID NO: 1161	30 aa
SEQ ID NO: 1163	MUC1F segment 7	90 nts
SEQ ID NO: 1164	Polypeptide encoded by SEQ ID NO: 1163	30 aa
SEQ ID NO: 1165	MUC1F segment 8	72 nts
SEQ ID NO: 1166	Polypeptide encoded by SEQ ID NO: 1165	24 aa
SEQ ID NO: 1167	MUC1R segment 1	90 nts
SEQ ID NO: 1168	Polypeptide encoded by SEQ ID NO: 1167	30 aa
SEQ ID NO: 1169	MUC1R segment 2	90 nts
SEQ ID NO: 1170	Polypeptide encoded by SEQ ID NO: 1169	30 aa
SEQ ID NO: 1171	MUC1R segment 3	90 nts
SEQ ID NO: 1172	Polypeptide encoded by SEQ ID NO: 1171	30 aa
SEQ ID NO: 1173	MUC1R segment 4	90 nts
SEQ ID NO: 1174	Polypeptide encoded by SEQ ID NO: 1173	30 aa

SEQUENCE ID	SEQUENCE	LINGTH
NUMBER	3) <u>- 19</u>	ibisavi Critici
SEQ ID NO: 1175	MUC1R segment 5	90 nts
SEQ ID NO: 1176	Polypeptide encoded by SEQ ID NO: 1175	30 aa
SEQ ID NO: 1177	MUC1R segment 6	90 nts
SEQ ID NO: 1178	Polypeptide encoded by SEQ ID NO: 1177	30 aa
SEQ ID NO: 1179	MUC1R segment 7	90 nts
SEQ ID NO: 1180	Polypeptide encoded by SEQ ID NO: 1179	30 aa
SEQ ID NO: 1181	MUC1R segment 8	90 nts
SEQ ID NO: 1182	Polypeptide encoded by SEQ ID NO: 1181	30 aa
SEQ ID NO: 1183	MUC1R segment 9	90 nts
SEQ ID NO: 1184	Polypeptide encoded by SEQ ID NO: 1183	30 aa
SEQ ID NO: 1185	MUC1R segment 10	90 nts .
SEQ ID NO: 1186	Polypeptide encoded by SEQ ID NO: 1185	30 aa
SEQ ID NO: 1187	MUC1R segment 11	90 nts
SEQ ID NO: 1188	Polypeptide encoded by SEQ ID NO: 1187	30 aa
SEQ ID NO: 1189	MUC1R segment 12	90 nts
SEQ ID NO: 1190	Polypeptide encoded by SEQ ID NO: 1189	30 aa
SEQ ID NO: 1191	MUC1R segment 13	90 nts
SEQ ID NO: 1192	Polypeptide encoded by SEQ ID NO: 1191	30 aa
SEQ ID NO: 1193	MUC1R segment 14	90 nts
SEQ ID NO: 1194	Polypeptide encoded by SEQ ID NO: 1193	30 aa
SEQ ID NO: 1195	MUC1R segment 15	90 nts
SEQ ID NO: 1196	Polypeptide encoded by SEQ ID NO: 1195	30 aa
SEQ ID NO: 1197	MUC1R segment 16	90 nts
SEQ ID NO: 1198	Polypeptide encoded by SEQ ID NO: 1197	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1199	MUC1R segment 17	90 nts
SEQ ID NO: 1200	Polypeptide encoded by SEQ ID NO: 1199	30 aa
SEQ ID NO: 1201	MUC1R segment 18	90 nts
SEQ ID NO: 1202	Polypeptide encoded by SEQ ID NO: 1201	30 aa
SEQ ID NO: 1203	MUC1R segment 19	90 nts
SEQ ID NO: 1204	Polypeptide encoded by SEQ ID NO: 1203	30 aa
SEQ ID NO: 1205	MUC1R segment 20	90 nts
SEQ ID NO: 1206	Polypeptide encoded by SEQ ID NO: 1205	30 aa
SEQ ID NO: 1207	MUC1R segment 21	48 nts
SEQ ID NO: 1208	Polypeptide encoded by SEQ ID NO: 1207	16 aa
SEQ ID NO: 1209	Differentiation Savine	16638 nts
SEQ ID NO: 1210	Polypeptide encoded by SEQ ID NO: 1209	5546 aa
SEQ ID NO: 1211	BAGE segment 1	90 nts
SEQ ID NO: 1212	Polypeptide encoded by SEQ ID NO: 1211	30 aa
SEQ ID NO: 1213	BAGE segment 2	90 nts
SEQ ID NO: 1214	Polypeptide encoded by SEQ ID NO: 1213	30 aa
SEQ ID NO: 1215	BAGE segment 3	51 nts
SEQ ID NO: 1216	Polypeptide encoded by SEQ ID NO: 1215	17 aa
SEQ ID NO: 1217	GAGE-1 segment 1	90 nts
SEQ ID NO: 1218	Polypeptide encoded by SEQ ID NO: 1217	30 aa
SEQ ID NO: 1219	GAGE-1 segment 2	90 nts
SEQ ID NO: 1220	Polypeptide encoded by SEQ ID NO: 1219	30 aa
SEQ ID NO: 1221	GAGE-1 segment 3	90 nts
SEQ ID NO: 1222	Polypeptide encoded by SEQ ID NO: 1221	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1223	GAGE-1 segment 4	90 nts
SEQ ID NO: 1224	Polypeptide encoded by SEQ ID NO: 1223	30 aa
SEQ ID NO: 1225	GAGE-1 segment 5	90 nts
SEQ ID NO: 1226	Polypeptide encoded by SEQ ID NO: 1225	30 aa
SEQ ID NO: 1227	GAGE-1 segment 6	90 nts
SEQ ID NO: 1228	Polypeptide encoded by SEQ ID NO: 1227	30 aa
SEQ ID NO: 1229	GAGE-1 segment 7	90 nts
SEQ ID NO: 1230	Polypeptide encoded by SEQ ID NO: 1229	30 aa
SEQ ID NO: 1231	GAGE-1 segment 8	90 nts
SEQ ID NO: 1232	Polypeptide encoded by SEQ ID NO: 1231	30 aa
SEQ ID NO: 1233	GAGE-1 segment 9	66 nts
SEQ ID NO: 1234	Polypeptide encoded by SEQ ID NO: 1233	22 aa
SEQ ID NO: 1235	gp100ln4 segment 1	90 nts
SEQ ID NO: 1236	Polypeptide encoded by SEQ ID NO: 1235	30 aa
SEQ ID NO: 1237	gp100ln4 segment 2	90 nts
SEQ ID NO: 1238	Polypeptide encoded by SEQ ID NO: 1237	30 aa
SEQ ID NO: 1239	gp100ln4 segment 3	75 nts
SEQ ID NO: 1240	Polypeptide encoded by SEQ ID NO: 1239	25 aa
SEQ ID NO: 1241	MAGE-1 segment 1	90 nts
SEQ ID NO: 1242	Polypeptide encoded by SEQ ID NO: 1241	30 aa
SEQ ID NO: 1243	MAGE-1 segment 2	90 nts
SEQ ID NO: 1244	Polypeptide encoded by SEQ ID NO: 1243	30 aa
SEQ ID NO: 1245	MAGE-1 segment 3	90 nts
SEQ ID NO: 1246	Polypeptide encoded by SEQ ID NO: 1245	30 aa

SEQUENCE LD NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1247	MAGE-1 segment 4	90 nts
SEQ ID NO: 1248	Polypeptide encoded by SEQ ID NO: 1247	30 aa
SEQ ID NO: 1249	MAGE-1 segment 5	90 nts
SEQ ID NO: 1250	Polypeptide encoded by SEQ ID NO: 1249	30 aa
SEQ ID NO: 1251	MAGE-1 segment 6	90 nts
SEQ ID NO: 1252	Polypeptide encoded by SEQ ID NO: 1251	30 aa
SEQ ID NO: 1253	MAGE-1 segment 7	90 nts
SEQ ID NO: 1254	Polypeptide encoded by SEQ ID NO: 1253	30 aa
SEQ ID NO: 1255	MAGE-1 segment 8	90 nts
SEQ ID NO: 1256	Polypeptide encoded by SEQ ID NO: 1255	30 aa
SEQ ID NO: 1257	MAGE-1 segment 9	90 nts
SEQ ID NO: 1258	Polypeptide encoded by SEQ ID NO: 1257	30 aa
SEQ ID NO: 1259	MAGE-1 segment 10	90 nts
SEQ ID NO: 1260	Polypeptide encoded by SEQ ID NO: 1259	30 aa
SEQ ID NO: 1261	MAGE-1 segment 11	90 nts
SEQ ID NO: 1262	Polypeptide encoded by SEQ ID NO: 1261	30 aa
SEQ ID NO: 1263	MAGE-1 segment 12	90 nts
SEQ ID NO: 1264	Polypeptide encoded by SEQ ID NO: 1263	30 aa
SEQ ID NO: 1265	MAGE-1 segment 13	90 nts
SEQ ID NO: 1266	Polypeptide encoded by SEQ ID NO: 1265	30 aa
SEQ ID NO: 1267	MAGE-1 segment 14	90 nts
SEQ ID NO: 1268	Polypeptide encoded by SEQ ID NO: 1267	30 aa
SEQ ID NO: 1269	MAGE-1 segment 15	90 nts
SEQ ID NO: 1270	Polypeptide encoded by SEQ ID NO: 1269	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH .
SEQ ID NO: 1271	MAGE-1 segment 16	90 nts
SEQ ID NO: 1272	Polypeptide encoded by SEQ ID NO: 1271	30 aa
SEQ ID NO: 1273	MAGE-1 segment 17	90 nts
SEQ ID NO: 1274	Polypeptide encoded by SEQ ID NO: 1273	30 aa
SEQ ID NO: 1275	MAGE-1 segment 18	90 nts
SEQ ID NO: 1276	Polypeptide encoded by SEQ ID NO: 1275	30 aa
SEQ ID NO: 1277	MAGE-1 segment 19	90 nts
SEQ ID NO: 1278	Polypeptide encoded by SEQ ID NO: 1277	30 aa
SEQ ID NO: 1279	MAGE-1 segment 20	84 nts
SEQ ID NO: 1280	Polypeptide encoded by SEQ ID NO: 1279	28 aa
SEQ ID NO: 1281	MAGE-3 segment 1	90 nts
SEQ ID NO: 1282	Polypeptide encoded by SEQ ID NO: 1281	30 aa
SEQ ID NO: 1283	MAGE-3 segment 2	90 nts
SEQ ID NO: 1284	Polypeptide encoded by SEQ ID NO: 1283	30 aa
SEQ ID NO: 1285	MAGE-3 segment 3	90 nts
SEQ ID NO: 1286	Polypeptide encoded by SEQ ID NO: 1285	30 aa
SEQ ID NO: 1287	MAGE-3 segment 4	90 nts
SEQ ID NO: 1288	Polypeptide encoded by SEQ ID NO: 1287	30 aa
SEQ ID NO: 1289	MAGE-3 segment 5	90 nts
SEQ ID NO: 1290	Polypeptide encoded by SEQ ID NO: 1289	30 aa
SEQ ID NO: 1291	MAGE-3 segment 6	90 nts
SEQ ID NO: 1292	Polypeptide encoded by SEQ ID NO: 1291	30 aa
SEQ ID NO: 1293	MAGE-3 segment 7	90 nts
SEQ ID NO: 1294	Polypeptide encoded by SEQ ID NO: 1293	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1295	MAGE-3 segment 8	90 nts
SEQ ID NO: 1296	Polypeptide encoded by SEQ ID NO: 1295	30 aa
SEQ ID NO: 1297	MAGE-3 segment 9	90 nts
SEQ ID NO: 1298	Polypeptide encoded by SEQ ID NO: 1297	30 aa
SEQ ID NO: 1299	MAGE-3 segment 10	90 nts
SEQ ID NO: 1300	Polypeptide encoded by SEQ ID NO: 1299	30 aa
SEQ ID NO: 1301	MAGE-3 segment 11	90 nts
SEQ ID NO: 1302	Polypeptide encoded by SEQ ID NO: 1301	30 aa
SEQ ID NO: 1303	MAGE-3 segment 12	90 nts
SEQ ID NO: 1304	Polypeptide encoded by SEQ ID NO: 1303	30 aa
SEQ ID NO: 1305	MAGE-3 segment 13	90 nts
SEQ ID NO: 1306	Polypeptide encoded by SEQ ID NO: 1305	30 aa
SEQ ID NO: 1307	MAGE-3 segment 14	90 nts
SEQ ID NO: 1308	Polypeptide encoded by SEQ ID NO: 1307	30 aa
SEQ ID NO: 1309	MAGE-3 segment 15	90 nts
SEQ ID NO: 1310	Polypeptide encoded by SEQ ID NO: 1309	30 aa
SEQ ID NO: 1311	MAGE-3 segment 16	90 nts
SEQ ID NO: 1312	Polypeptide encoded by SEQ ID NO: 1311	30 aa
SEQ ID NO: 1313	MAGE-3 segment 17	90 nts
SEQ ID NO: 1314	Polypeptide encoded by SEQ ID NO: 1313	30 aa
SEQ ID NO: 1315	MAGE-3 segment 18	90 nts
SEQ ID NO: 1316	Polypeptide encoded by SEQ ID NO: 1315	30 aa
SEQ ID NO: 1317	MAGE-3 segment 19	90 nts
SEQ ID NO: 1318	Polypeptide encoded by SEQ ID NO: 1317	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1319	MACE 2 20	00
	MAGE-3 segment 20	90 nts
SEQ ID NO: 1320	Polypeptide encoded by SEQ ID NO: 1319	30 aa
SEQ ID NO: 1321	MAGE-3 segment 21	54 nts
SEQ ID NO: 1322	Polypeptide encoded by SEQ ID NO: 1321	18 aa
SEQ ID NO: 1323	PRAME segment 1	90 nts
SEQ ID NO: 1324	Polypeptide encoded by SEQ ID NO: 1323	30 aa
SEQ ID NO: 1325	PRAME segment 2	90 nts
SEQ ID NO: 1326	Polypeptide encoded by SEQ ID NO: 1325	30 aa
SEQ ID NO: 1327	PRAME segment 3	90 nts
SEQ ID NO: 1328	Polypeptide encoded by SEQ ID NO: 1327	30 aa
SEQ ID NO: 1329	PRAME segment 4 .	90 nts
SEQ ID NO: 1330	Polypeptide encoded by SEQ ID NO: 1329	30 aa
SEQ ID NO: 1331	PRAME segment 5	90 nts
SEQ ID NO: 1332	Polypeptide encoded by SEQ ID NO: 1331	30 aa
SEQ ID NO: 1333	PRAME segment 6	90 nts
SEQ ID NO: 1334	Polypeptide encoded by SEQ ID NO: 1333	30 aa
SEQ ID NO: 1335	PRAME segment 7	90 nts
SEQ ID NO: 1336	Polypeptide encoded by SEQ ID NO: 1335	30 aa
SEQ ID NO: 1337	PRAME segment 8	90 nts
SEQ ID NO: 1338	Polypeptide encoded by SEQ ID NO: 1337	30 aa
SEQ ID NO: 1339	PRAME segment 9	90 nts
SEQ ID NO: 1340	Polypeptide encoded by SEQ ID NO: 1339	30 aa
SEQ ID NO: 1341	PRAME segment 10	90 nts
SEQ ID NO: 1342	Polypeptide encoded by SEQ ID NO: 1341	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1343	PRAME segment 11	90 nts
SEQ ID NO: 1344	Polypeptide encoded by SEQ ID NO: 1343	30 aa
SEQ ID NO: 1345	PRAME segment 12	90 nts
SEQ ID NO: 1346	Polypeptide encoded by SEQ ID NO: 1345	30 aa
SEQ ID NO: 1347	PRAME segment 13	90 nts
SEQ ID NO: 1348	Polypeptide encoded by SEQ ID NO: 1347	30 aa
SEQ ID NO: 1349	PRAME segment 14	90 nts
SEQ ID NO: 1350	Polypeptide encoded by SEQ ID NO: 1349	30 aa
SEQ ID NO: 1351	PRAME segment 15	90 nts
SEQ ID NO: 1352	Polypeptide encoded by SEQ ID NO: 1351	30 aa
SEQ ID NO: 1353	PRAME segment 16.	90 nts
SEQ ID NO: 1354	Polypeptide encoded by SEQ ID NO: 1353	30 aa
SEQ ID NO: 1355	PRAME segment 17	90 nts
SEQ ID NO: 1356	Polypeptide encoded by SEQ ID NO: 1355	30 aa
SEQ ID NO: 1357	PRAME segment 18	90 nts
SEQ ID NO: 1358	Polypeptide encoded by SEQ ID NO: 1357	30 aa
SEQ ID NO: 1359	PRAME segment 19	90 nts
SEQ ID NO: 1360	Polypeptide encoded by SEQ ID NO: 1359	30 aa
SEQ ID NO: 1361	PRAME segment 20	90 nts
SEQ ID NO: 1362	Polypeptide encoded by SEQ ID NO: 1361	30 aa
SEQ ID NO: 1363	PRAME segment 21	90 nts
SEQ ID NO: 1364	Polypeptide encoded by SEQ ID NO: 1363	30 aa
SEQ ID NO: 1365	PRAME segment 22	90 nts
SEQ ID NO: 1366	Polypeptide encoded by SEQ ID NO: 1365	30 aa

SEQUENCE ID NUMBER	SEQUENCS	LENGTH
SEQ ID NO: 1367	PRAME segment 23	90 nts
SEQ ID NO: 1368	Polypeptide encoded by SEQ ID NO: 1367	30 aa
SEQ ID NO: 1369	PRAME segment 24	90 nts
SEQ ID NO: 1370	Polypeptide encoded by SEQ ID NO: 1369	30 aa
SEQ ID NO: 1371	PRAME segment 25	90 nts
SEQ ID NO: 1372	Polypeptide encoded by SEQ ID NO: 1371	30 aa
SEQ ID NO: 1373	PRAME segment 26	90 nts
SEQ ID NO: 1374	Polypeptide encoded by SEQ ID NO: 1373	30 aa
SEQ ID NO: 1375	PRAME segment 27	90 nts
SEQ ID NO: 1376	Polypeptide encoded by SEQ ID NO: 1375	30 aa
SEQ ID NO: 1377	PRAME segment 28	90 nts
SEQ ID NO: 1378	Polypeptide encoded by SEQ ID NO: 1377	30 aa
SEQ ID NO: 1379	PRAME segment 29	90 nts
SEQ ID NO: 1380	Polypeptide encoded by SEQ ID NO: 1379	30 aa
SEQ ID NO: 1381	PRAME segment 30	90 nts
SEQ ID NO: 1382	Polypeptide encoded by SEQ ID NO: 1381	30 aa
SEQ ID NO: 1383	PRAME segment 31	90 nts
SEQ ID NO: 1384	Polypeptide encoded by SEQ ID NO: 1383	30 aa
SEQ ID NO: 1385	PRAME segment 32	90 nts .
SEQ ID NO: 1386	Polypeptide encoded by SEQ ID NO: 1385	30 aa
SEQ ID NO: 1387	PRAME segment 33	90 nts
SEQ ID NO: 1388	Polypeptide encoded by SEQ ID NO: 1387	30 aa
SEQ ID NO: 1389	PRAME segment 34	54 nts
SEQ ID NO: 1390	Polypeptide encoded by SEQ ID NO: 1389	18 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1391	TRP2IN2 segment 1	90 nts
SEQ ID NO: 1392	Polypeptide encoded by SEQ ID NO: 1391	30 aa
SEQ ID NO: 1393	TRP2IN2 segment 2	90 nts
SEQ ID NO: 1394	Polypeptide encoded by SEQ ID NO: 1393	30 aa
SEQ ID NO: 1395	TRP2IN2 segment 3	84 nts
SEQ ID NO: 1396	Polypeptide encoded by SEQ ID NO: 1395	28 aa
SEQ ID NO: 1397	NYNSO1a segment 1	90 nts
SEQ ID NO: 1398	Polypeptide encoded by SEQ ID NO: 1397	30 aa
SEQ ID NO: 1399	NYNSO1a segment 2	90 nts
SEQ ID NO: 1400	Polypeptide encoded by SEQ ID NO: 1399	30 aa
SEQ ID NO: 1401	NYNSO1a segment 3	90 nts
SEQ ID NO: 1402	Polypeptide encoded by SEQ ID NO: 1401	30 aa
SEQ ID NO: 1403	NYNSO1a segment 4	90 nts
SEQ ID NO: 1404	Polypeptide encoded by SEQ ID NO: 1403	30 aa
SEQ ID NO: 1405	NYNSO1a segment 5	90 nts
SEQ ID NO: 1406	Polypeptide encoded by SEQ ID NO: 1405	30 aa
SEQ ID NO: 1407	NYNSO1a segment 6	90 nts
SEQ ID NO: 1408	Polypeptide encoded by SEQ ID NO: 1407	30 aa
SEQ ID NO: 1409	NYNSO1a segment 7	90 nts
SEQ ID NO: 1410	Polypeptide encoded by SEQ ID NO: 1409	30 aa
SEQ ID NO: 1411	NYNSO1a segment 8	90 nts
SEQ ID NO: 1412	Polypeptide encoded by SEQ ID NO: 1411	30 aa
SEQ ID NO: 1413	NYNSO1a segment 9	90 nts
SEQ ID NO: 1414	Polypeptide encoded by SEQ ID NO: 1413	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1415	NYNSO1a segment 10	90 nts
SEQ ID NO: 1416	Polypeptide encoded by SEQ ID NO: 1415	30 aa
SEQ ID NO: 1417	NYNSO1a segment 11	90 nts
SEQ ID NO: 1418	Polypeptide encoded by SEQ ID NO: 1417	30 aa
SEQ ID NO: 1419	NYNSO1a segment 12	57 nts
SEQ ID NO: 1420	Polypeptide encoded by SEQ ID NO: 1419	19 aa
SEQ ID NO: 1421	NYNSO1b segment 1	90 nts
SEQ ID NO: 1422	Polypeptide encoded by SEQ ID NO: 1421	30 aa
<b>SEQ ID NO: 1423</b>	NYNSO1b segment 2	90 nts
SEQ ID NO: 1424	Polypeptide encoded by SEQ ID NO: 1423	30 aa
SEQ ID NO: 1425	NYNSO1b segment 3	90 nts
SEQ ID NO: 1426	Polypeptide encoded by SEQ ID NO: 1425	30 aa
SEQ ID NO: 1427	NYNSO1b segment 4	51 nts
SEQ ID NO: 1428	Polypeptide encoded by SEQ ID NO: 1427	
SEQ ID NO: 1429	LAGE1 segment 1	90 nts
SEQ ID NO: 1430	Polypeptide encoded by SEQ ID NO: 1429	30 aa
SEQ ID NO: 1431	LAGE1 segment 2	90 nts
SEQ ID NO: 1432	Polypeptide encoded by SEQ ID NO: 1431	30 aa
SEQ ID NO: 1433	LAGE1 segment 3	90 nts
SEQ ID NO: 1434	Polypeptide encoded by SEQ ID NO: 1433	30 aa
SEQ ID NO: 1435	LAGE1 segment 4	90 nts
SEQ ID NO: 1436	Polypeptide encoded by SEQ ID NO: 1435	30 aa
SEQ ID NO: 1437	LAGE1 segment 5	90 nts
SEQ ID NO: 1438	Polypeptide encoded by SEQ ID NO: 1437	30 aa

SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1439	LAGE1 segment 6	90 nts
SEQ ID NO: 1440	Polypeptide encoded by SEQ ID NO: 1439	30 aa
SEQ ID NO: 1441	LAGE1 segment 7	90 nts
SEQ ID NO: 1442	Polypeptide encoded by SEQ ID NO: 1441	30 aa
SEQ ID NO: 1443	LAGE1 segment 8	90 nts
SEQ ID NO: 1444	Polypeptide encoded by SEQ ID NO: 1443	30 aa
SEQ ID NO: 1445	LAGE1 segment 9	90 nts
SEQ ID NO: 1446	Polypeptide encoded by SEQ ID NO: 1445	30 aa
SEQ ID NO: 1447	LAGE1 segment 10	90 nts
SEQ ID NO: 1448	Polypeptide encoded by SEQ ID NO: 1447	30 aa
SEQ ID NO: 1449	LAGE1 segment 11	90 nts
SEQ ID NO: 1450	Polypeptide encoded by SEQ ID NO: 1449 30 as	
SEQ ID NO: 1451	LAGE1 segment 12	57 nts
SEQ ID NO: 1452	Polypeptide encoded by SEQ ID NO: 1451	19 aa
SEQ ID NO: 1453	Melanoma cancer specific Savine	10623 nts
SEQ ID NO: 1454	Polypeptide encoded by SEQ ID NO: 1453	3541 aa
SEQ ID NO: 1455	Figure 16 A1S1 99mer	99 nts
SEQ ID NO: 1456	Figure 16 A1S2 100mer	100 nts
SEQ ID NO: 1457	Figure 16 A1S3 100mer	100 nts
SEQ ID NO: 1458	Figure 16 A1S4 100mer	100 nts
SEQ ID NO: 1459	Figure 16 A1S5 100mer	100 nts
SEQ ID NO: 1460	Figure 16 A1S6 99mer	99 nts
SEQ ID NO: 1461	Figure 16 A1S7 97mer	99 nts
SEQ ID NO: 1462	Figure 16 A1S8 100mer	100 nts

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SEQUENCE ID NUMBER	SEQUENCE	LENGTH
SEQ ID NO: 1463	Figure 16 A1S9 100mer	100 nts
SEQ ID NO: 1464	Figure 16 A1S10 75mer	76 nts
SEQ ID NO: 1465	Figure 16 A1F 20mer	20 nts
SEQ ID NO: 1466	Figure 16 A1R 20mer	20 nts
SEQ ID NO: 1467	Amino acid sequence of immunostimulatory domain of an invasin protein from Yersinia spp.	16 aa

#### **DETAILED DESCRIPTION OF THE INVENTION**

## 1. Definitions

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The articles "a" and "an" are used herein to refer to one or to more than one (i.e., to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element.

As used herein, the term "about" refers to a quantity, level, value, dimension, size, or amount that varies by as much as 30%, preferably by as much as 20%, and more preferably by as much as 10% to a reference quantity, level, value, dimension, size, or amount.

By "antigen-binding molecule" is meant a molecule that has binding affinity for a target antigen. It will be understood that this term extends to immunoglobulins, immunoglobulin fragments and non-immunoglobulin derived protein frameworks that exhibit antigen-binding activity.

The term "clade" as used herein refers to a hypothetical species of an organism and its descendants or a monophyletic group of organisms. Clades carry a definition, based on ancestry, and a diagnosis, based on synapomorphies. It should be noted that diagnoses of clades could change while definitions do not.

Throughout this specification, unless the context requires otherwise, the words "comprise", "comprises" and "comprising" will be understood to imply the inclusion of a stated step or element or group of steps or elements but not the exclusion of any other step or element or group of steps or elements.

By "expression vector" is meant any autonomous genetic element capable of directing the synthesis of a protein encoded by the vector. Such expression vectors are known by practitioners in the art.

As used herein, the term "function" refers to a biological, enzymatic, or therapeutic function.

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"Homology" refers to the percentage number of amino acids that are identical or constitute conservative substitutions as defined in Table B infra. Homology may be determined using sequence comparison programs such as GAP (Deveraux et al. 1984, Nucleic Acids Research 12, 387-395). In this way, sequences of a similar or substantially different length to those cited herein might be compared by insertion of gaps into the alignment, such gaps being determined, for example, by the comparison algorithm used by GAP.

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To enhance an immune response ("immunoenhancement"), as is well-known in the art, means to increase an animal's capacity to respond to foreign or disease-specific antigens (e.g., cancer antigens) i.e., those cells primed to attack such antigens are increased in number, activity, and ability to detect and destroy the those antigens. Strength of immune response is measured by standard tests including: direct measurement of peripheral blood lymphocytes by means known to the art; natural killer cell cytotoxicity assays (see, e.g., Provinciali M. et al (1992, J. Immunol. Meth. 155: 19-24), cell proliferation assays (see, e.g., Vollenweider, I. and Groseurth, P. J. (1992, J. Immunol. Meth. 149: 133-135), immunoassays of immune cells and subsets (see, e.g., Loeffler, D. A., et al. (1992, Cytom. 13: 169-174); Rivoltini, L., et al. (1992, Can. Immunol. Immunother. 34: 241-251); or skin tests for cell-mediated immunity (see, e.g., Chang, A. E. et al (1993, Cancer Res. 53: 1043-1050). Any statistically significant increase in strength of immune response as measured by the foregoing tests is considered "enhanced immune response" "immunoenhancement" or "immunopotentiation" as used herein. Enhanced immune response is also indicated by physical manifestations such as fever and inflammation, as well as healing of systemic and local infections, and reduction of symptoms in disease, i.e., decrease in tumour size, alleviation of symptoms of a disease or 25 condition including, but not restricted to, leprosy, tuberculosis, malaria, naphthous ulcers, herpetic and papillomatous warts, gingivitis, artherosclerosis, the concomitants of AIDS such as Kaposi's sarcoma, bronchial infections, and the like. Such physical manifestations also define "enhanced immune response" "immunoenhancement" or "immunopotentiation" as used herein.

30 Reference herein to "immuno-interactive" includes reference to any interaction. reaction, or other form of association between molecules and in particular where one of the molecules is, or mimics, a component of the immune system.

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By "isolated" is meant material that is substantially or essentially free from components that normally accompany it in its native state.

By "modulating" is meant increasing or decreasing, either directly or indirectly, an immune response against a target antigen of a member selected from the group consisting of a cancer and an organism, preferably a pathogenic organism.

By "natural gene" is meant a gene that naturally encodes a protein.

The term "natural polypeptide" as used herein refers to a polypeptide that exists in nature.

By "obtained from" is meant that a sample such as, for example, a polynucleotide extract or polypeptide extract is isolated from, or derived from, a particular source of the host. For example, the extract can be obtained from a tissue or a biological fluid isolated directly from the host.

The term "oligonucleotide" as used herein refers to a polymer composed of a multiplicity of nucleotide residues (deoxyribonucleotides or ribonucleotides, or related structural variants or synthetic analogues thereof) linked via phosphodiester bonds (or related structural variants or synthetic analogues thereof). Thus, while the term "oligonucleotide" typically refers to a nucleotide polymer in which the nucleotide residues and linkages between them are naturally occurring, it will be understood that the term also includes within its scope various analogues including, but not restricted to, peptide nucleic acids (PNAs), phosphoramidates, phosphorothioates, methyl phosphonates, 2-O-methyl ribonucleic acids, and the like. The exact size of the molecule can vary depending on the particular application. An oligonucleotide is typically rather short in length, generally from about 10 to 30 nucleotide residues, but the term can refer to molecules of any length, although the term "polynucleotide" or "nucleic acid" is typically used for large oligonucleotides.

By "operably linked" is meant that transcriptional and translational regulatory polynucleotides are positioned relative to a polypeptide-encoding polynucleotide in such a manner that the polynucleotide is transcribed and the polypeptide is translated.

The term "parent polypeptide" as used herein typically refers to a polypeptide encoded by a natural gene. However, it is possible that the parent polypeptide corresponds to a protein that is not naturally-occurring but has been engineered using recombinant techniques. In this instance, a polynucleotide encoding the parent polypeptide may 5 comprise different but synonymous codons relative to a natural gene encoding the same polypeptide. Alternatively, the parent polypeptide may not correspond to a natural polypeptide sequence. For example, the parent polypeptide may comprise one or more consensus sequences common to a plurality of polypeptides.

The term "patient" refers to patients of human or other mammal and includes any individual it is desired to examine or treat using the methods of the invention. However, it will be understood that "patient" does not imply that symptoms are present. Suitable mammals that fall within the scope of the invention include, but are not restricted to. primates, livestock animals (e.g., sheep, cows, horses, donkeys, pigs), laboratory test animals (e.g., rabbits, mice, rats, guinea pigs, hamsters), companion animals (e.g., cats, dogs) and captive wild animals (e.g., foxes, deer, dingoes). 15

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By "pharmaceutically-acceptable carrier" is meant a solid or liquid filler, diluent or encapsulating substance that can be safely used in topical or systemic administration to a mammal.

"Polypeptide", "peptide" and "protein" are used interchangeably herein to refer to a polymer of amino acid residues and to variants and synthetic analogues of the same. Thus, these terms apply to amino acid polymers in which one or more amino acid residues is a synthetic non-naturally occurring amino acid, such as a chemical analogue of a corresponding naturally occurring amino acid, as well as to naturally-occurring amino acid polymers.

The term "polynucleotide" or "nucleic acid" as used herein designates mRNA, RNA, cRNA, cDNA or DNA. The term typically refers to oligonucleotides greater than 30 nucleotide residues in length.

By "primer" is meant an oligonucleotide which, when paired with a strand of DNA, is capable of initiating the synthesis of a primer extension product in the presence of a suitable polymerising agent. The primer is preferably single-stranded for maximum

efficiency in amplification but can alternatively be double-stranded. A primer must be sufficiently long to prime the synthesis of extension products in the presence of the polymerisation agent. The length of the primer depends on many factors, including application, temperature to be employed, template reaction conditions, other reagents, and source of primers. For example, depending on the complexity of the target sequence, the oligonucleotide primer typically contains 15 to 35 or more nucleotide residues, although it can contain fewer nucleotide residues. Primers can be large polynucleotides, such as from about 35 nucleotides to several kilobases or more. Primers can be selected to be "substantially complementary" to the sequence on the template to which it is designed to hybridise and serve as a site for the initiation of synthesis. By "substantially complementary", it is meant that the primer is sufficiently complementary to hybridise with a target polynucleotide. Preferably, the primer contains no mismatches with the template to which it is designed to hybridise but this is not essential. For example, noncomplementary nucleotide residues can be attached to the 5' end of the primer, with the 15 remainder of the primer sequence being complementary to the template. Alternatively, non-complementary nucleotide residues or a stretch of non-complementary nucleotide residues can be interspersed into a primer, provided that the primer sequence has sufficient complementarity with the sequence of the template to hybridise therewith and thereby form a template for synthesis of the extension product of the primer.

"Probe" refers to a molecule that binds to a specific sequence or sub-sequence or other moiety of another molecule. Unless otherwise indicated, the term "probe" typically refers to a polynucleotide probe that binds to another polynucleotide, often called the "target polynucleotide", through complementary base pairing. Probes can bind target polynucleotides lacking complete sequence complementarity with the probe, depending on the stringency of the hybridisation conditions. Probes can be labelled directly or indirectly.

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By "recombinant polypeptide" is meant a polypeptide made using recombinant techniques, i.e., through the expression of a recombinant or synthetic polynucleotide.

Terms used to describe sequence relationships between two or more polynucleotides or polypeptides include "reference sequence", "comparison window", "sequence identity", "percentage of sequence identity" and "substantial identity". A "reference sequence" is at least 12 but frequently 15 to 18 and often at least 25 monomer

units, inclusive of nucleotides and amino acid residues, in length. Because two polynucleotides may each comprise (1) a sequence (i.e., only a portion of the complete polynucleotide sequence) that is similar between the two polynucleotides, and (2) a sequence that is divergent between the two polynucleotides, sequence comparisons between two (or more) polynucleotides are typically performed by comparing sequences of the two polynucleotides over a "comparison window" to identify and compare local regions of sequence similarity. A "comparison window" refers to a conceptual segment of at least 50 contiguous positions, usually about 50 to about 100, more usually about 100 to about 150 in which a sequence is compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned. The comparison window may comprise additions or deletions (i.e., gaps) of about 20% or less as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. Optimal alignment of sequences for aligning a comparison window may be conducted by computerised implementations of algorithms (GAP, 15 BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package Release 7.0, Genetics Computer Group, 575 Science Drive Madison, WI, USA) or by inspection and the best alignment (i.e., resulting in the highest percentage homology over the comparison window) generated by any of the various methods selected. Reference also may be made to the BLAST family of programs as for example disclosed by Altschul et al., 1997, Nucl. Acids Res. 25:3389. A detailed discussion of sequence analysis can be found in Unit 19.3 of Ausubel et al., "Current Protocols in Molecular Biology", John Wiley & Sons Inc, 1994-1998, Chapter 15.

The term "sequence identity" as used herein refers to the extent that sequences are identical on a nucleotide-by-nucleotide basis or an amino acid-by-amino acid basis over a window of comparison. Thus, a "percentage of sequence identity" is calculated by comparing two optimally aligned sequences over the window of comparison, determining the number of positions at which the identical nucleic acid base (e.g., A, T, C, G, I) or the identical amino acid residue (e.g., Ala, Pro, Ser, Thr, Gly, Val, Leu, Ile, Phe, Tyr, Trp, Lys, Arg, His, Asp, Glu, Asn, Gln, Cys and Met) occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison (i.e., the window size), and multiplying the result by 100 to yield the percentage of sequence identity. For the purposes of the present

invention, "sequence identity" will be understood to mean the "match percentage" calculated by the DNASIS computer program (Version 2.5 for windows; available from Hitachi Software engineering Co., Ltd., South San Francisco, California, USA) using standard defaults as used in the reference manual accompanying the software.

The term "synthetic polynucleotide" as used herein refers to a polynucleotide formed in vitro by the manipulation of a polynucleotide into a form not normally found in nature. For example, the synthetic polynucleotide can be in the form of an expression vector. Generally, such expression vectors include transcriptional and translational regulatory polynucleotide operably linked to the polynucleotide.

The term "synonymous codon" as used herein refers to a codon having a different nucleotide sequence than another codon but encoding the same amino acid as that other codon.

By "translational efficiency" is meant the efficiency of a cell's protein synthesis machinery to incorporate the amino acid encoded by a codon into a nascent polypeptide chain. This efficiency can be evidenced, for example, by the rate at which the cell is able to synthesise the polypeptide from an RNA template comprising the codon, or by the amount of the polypeptide synthesised from such a template.

By "vector" is meant a polynucleotide molecule, preferably a DNA molecule derived, for example, from a plasmid, bacteriophage, yeast or virus, into which a polynucleotide can be inserted or cloned. A vector preferably contains one or more unique restriction sites and can be capable of autonomous replication in a defined host cell including a target cell or tissue or a progenitor cell or tissue thereof, or be integrable with the genome of the defined host such that the cloned sequence is reproducible. Accordingly, the vector can be an autonomously replicating vector, i.e., a vector that exists as an extrachromosomal entity, the replication of which is independent of chromosomal replication, e.g., a linear or closed circular plasmid, an extrachromosomal element, a minichromosome, or an artificial chromosome. The vector can contain any means for assuring self-replication. Alternatively, the vector can be one which, when introduced into the host cell, is integrated into the genome and replicated together with the chromosome(s) into which it has been integrated. A vector system can comprise a single vector or plasmid, two or more vectors or plasmids, which together contain the total DNA to be introduced

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into the genome of the host cell, or a transposon. The choice of the vector will typically depend on the compatibility of the vector with the host cell into which the vector is to be introduced. In the present case, the vector is preferably a viral or viral-derived vector, which is operably functional in animal and preferably mammalian cells. Such vector may be derived from a poxvirus, an adenovirus or yeast. The vector can also include a selection marker such as an antibiotic resistance gene that can be used for selection of suitable transformants. Examples of such resistance genes are known to those of skill in the art and include the *nptII* gene that confers resistance to the antibiotics kanamycin and G418 (Geneticin®) and the *hph* gene which confers resistance to the antibiotic hygromycin B.

#### 2. Synthetic polypeptides

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The inventors have surprisingly discovered that the structure of a parent polypeptide can be disrupted sufficiently to impede, abrogate or otherwise alter at least one function of the parent polypeptide, while simultaneously minimising the destruction of potentially useful epitopes that are present in the parent polypeptide, by fusing, coupling or otherwise linking together different segments of the parent polypeptide in a different relationship relative to their linkage in the parent polypeptide. As a result of this change in relationship, the sequence of the linked segments in the resulting synthetic polypeptide is different to a sequence contained within the parent polypeptide. The synthetic polypeptides 10 of the invention are useful as immunopotentiating agents, and are referred to elsewhere in the specification as scrambled antigen vaccines, super attenuated vaccines or "Savines".

Thus, the invention broadly resides in a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein said segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide.

It is preferable but not essential that the segments in said synthetic polypeptide are linked sequentially in a different order or arrangement relative to that of corresponding segments in said at least one parent polypeptide. For example, in the case of a parent polypeptide that comprises three contiguous or overlapping segments A-B-C-D, these segments may be linked in 23 other possible orders to form a synthetic polypeptide. These orders may be selected from the group consisting of: A-B-D-C, A-C-B-D, A-C-D-B, A-D-B-C, A-D-C-B, B-A-C-D, B-A-D-C, B-C-A-D, B-C-D-A, B-D-A-C, B-D-C-A, C-A-B-D, C-A-D-B, C-B-A-D, C-B-D-A, C-D-A-B, C-D-B-A, D-A-B-C, D-A-C-B, D-B-A-C, D-B-C-A, D-C-A-B, and D-C-B-A. Although the rearrangement of the segments is preferably 25 random, it is especially preferable to exclude or otherwise minimise rearrangements that result in complete or partial reassembly of the parent sequence (e.g., ADBC, BACD, DABC). It will be appreciated, however, that the probability of such complete or partial reassembly diminishes as the number of segments for rearrangement increases.

The order of the segments is suitably shuffled, reordered or otherwise rearranged relative to the order in which they exist in the parent polypeptide so that the structure of the polypeptide is disrupted sufficiently to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide. Preferably, the segments of the parent polypeptide are randomly rearranged in the synthetic polypeptide.

The parent polypeptide is suitably a polypeptide that is associated with a disease or condition. For example, the parent polypeptide may be a polypeptide expressed by a pathogenic organism or a cancer. Alternatively, the parent polypeptide can be a self peptide related to an autoimmune disease including, but are not limited to, diseases such as diabetes (e.g., juvenile diabetes), multiple sclerosis, rheumatoid arthritis, myasthenia gravis, atopic dermatitis, and psoriasis and ankylosing spondylitis. Accordingly, the synthetic molecules of the present invention may also have utility for the induction of tolerance in a subject afflicted with an autoimmune disease or condition or with an allergy or other condition to which tolerance is desired. For example tolerance may be induced by contacting an immature dendritic cell of the individual to be treated with a synthetic polypeptide of the invention or by expressing in an immature dendritic cell a synthetic polynucleotide of the invention. Tolerance may also be induced against antigens causing allergic responses (e.g., asthma, hay fever). In this case, the parent polypeptide is suitably an allergenic protein including, but not restricted to, house-dust-mite allergenic proteins as for example described by Thomas and Smith (1998, Allergy, 53(9): 821-832).

The pathogenic organism includes, but is not restricted to, yeast, a virus, a bacterium, and a parasite. Any natural host of the pathogenic organism is contemplated by the present invention and includes, but is not limited to, mammals, avians and fish. In a preferred embodiment, the pathogenic organism is a virus, which may be an RNA virus or a DNA virus. Preferably, the RNA virus is Human Immunodeficiency Virus (HIV), Poliovirus, and Influenza virus, Rous sarcoma virus, or a Flavivirus such as Japanese encephalitis virus. In a preferred embodiment, the RNA virus is a Hepatitis virus including, 25 but not limited to, Hepatitis strains A, B and C. Suitably, the DNA virus is a Herpesvirus including, but not limited to, Herpes simplex virus, Epstein-Barr virus, Cytomegalovirus and Parvovirus. In a preferred embodiment, the virus is HIV and the parent polypeptide is suitably selected from env, gag, pol, vif, vpr, tat, rev, vpu and nef, or combination thereof. In an alternate preferred embodiment, the virus is Hepatitis Cla virus and the parent polypeptide is the Hepatitis Cla virus polyprotein.

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In another embodiment, the pathogenic organism is a bacterium, which includes, but is not restricted to, Neisseria species, Meningococcal species, Haemophilus species Salmonella species, Streptococcal species, Legionella species and Mycobacterium species.

In yet another embodiment, the pathogenic organism is a parasite, which includes, but is not restricted to, *Plasmodium* species, *Schistosoma* species, *Leishmania* species, *Trypanosoma* species, *Toxoplasma* species and *Giardia* species.

Any cancer or tumour is contemplated by the present invention. For example, the cancer or tumour includes, but is not restricted to, melanoma, lung cancer, breast cancer, cervical cancer, prostate cancer, colon cancer, pancreatic cancer, stomach cancer, bladder cancer, kidney cancer, post transplant lymphoproliferative disease (PTLD), Hodgkin's Lymphoma and the like. Preferably, the cancer or tumour relates to melanoma. In a preferred embodiment of this type, the parent polypeptide is a melanocyte differentiation antigen which is suitably selected from gp100, MART, TRP-1, Tyros, TRP2, MC1R, MUC1F, MUC1R or a combination thereof. In an alternate preferred embodiment of this type, the parent polypeptide is a melanoma-specific antigen which is suitably selected from BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b, LAGE1 or a combination thereof.

In a preferred embodiment, the segments are selected on the basis of size. A segment according to the invention may be of any suitable size that can be utilised to elicit an immune response against an antigen encoded by the parent polypeptide. A number of factors can influence the choice of segment size. For example, the size of a segment should be preferably chosen such that it includes, or corresponds to the size of, T cell epitopes and their processing requirement. Practitioners in the art will recognise that class I-restricted T cell epitopes can be between 8 and 10 amino acids in length and if placed next to unnatural flanking residues, such epitopes can generally require 2 to 3 natural flanking amino acids to ensure that they are efficiently processed and presented. Class II-restricted T cell epitopes can range between 12 and 25 amino acids in length and may not require natural flanking residues for efficient proteolytic processing although it is believed that natural flanking residues may play a role. Another important feature of class II-restricted epitopes is that they generally contain a core of 9-10 amino acids in the middle which bind specifically to class II MHC molecules with flanking sequences either side of this core

stabilising binding by associating with conserved structures on either side of class II MHC antigens in a sequence independent manner (Brown et al., 1993). Thus the functional region of class II-restricted epitopes is typically less than 15 amino acids long. The size of linear B cell epitopes and the factors effecting their processing, like class II-restricted epitopes, are quite variable although such epitopes are frequently smaller in size than 15 amino acids. From the foregoing, it is preferable, but not essential, that the size of the segment is at least 4 amino acids, preferably at least 7 amino acids, more preferably at least 12 amino acids, more preferably at least 20 amino acids and more preferably at least 30 amino acids. Suitably, the size of the segment is less than 2000 amino acids, more preferably less than 1000 amino acids, more preferably less than 500 amino acids, more preferably less than 200 amino acids, more preferably less than 100 amino acids, more preferably less than 80 amino acids and even more preferably less than 60 amino acids and still even more preferably less than 40 amino acids. In this regard, it is preferable that the size of the segments is as small as possible so that the synthetic polypeptide adopts a 15 functionally different structure relative to the structure of the parent polypeptide. It is also preferable that the size of the segments is large enough to minimise loss of T cell epitopes. In an especially preferred embodiment, the size of the segment is about 30 amino acids.

An optional spacer may be utilised to space adjacent segments relative to each other. Accordingly, an optional spacer may be interposed between some or all of the segments. The spacer suitably alters proteolytic processing and/or presentation of adjacent segment(s). In a preferred embodiment of this type, the spacer promotes or otherwise enhances proteolytic processing and/or presentation of adjacent segment(s). Preferably, the spacer comprises at least one amino acid. The at least one amino acid is suitably a neutral amino acid. The neutral amino acid is preferably alanine. Alternatively, the at least one amino acid is cysteine.

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In a preferred embodiment, segments are selected such that they have partial sequence identity or homology with one or more other segments. Suitably, at one or both ends of a respective segment there is comprised at least 4 contiguous amino acids, preferably at least 7 contiguous amino acids, more preferably at least 10 contiguous amino acids, more preferably at least 15 contiguous amino acids and even more preferably at least 20 contiguous amino acids that are identical to, or homologous with, an amino acid sequence contained within one or more other of said segments. Preferably, at the or each

end of a respective segment there is comprised less than 500 contiguous amino acids, more preferably less than 200 contiguous amino acids, more preferably less than 100 contiguous amino acids, more preferably less than 50 contiguous amino acids, more preferably less than 40 contiguous amino acids, and even more preferably less than 30 contiguous amino acids that are identical to, or homologous with, an amino acid sequence contained within one or more other of said segments. Such sequence overlap (also referred to elsewhere in the specification as "overlapping fragments" or "overlapping segments") is preferable to ensure potential epitopes at segment boundaries are not lost and to ensure that epitopes at or near segment boundaries are processed efficiently if placed beside or near amino acids that inhibit processing. Preferably, the segment size is about twice the size of the overlap.

In a preferred embodiment, when segments have partial sequence homology therebetween, the homologous sequences suitably comprise conserved and/or non-conserved amino acid differences. Exemplary conservative substitutions are listed in the following table.

#### 15 *TABLE B*

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Crignal Residue	Inaugian, Suksikations
Ala	Ser
Arg	Lys
Asn	Gln, His
Asp	Glu
Cys	Ser
Gln	Asn
Glu	Asp
Gly	Pro
His	Asn, Gln
Ile ·	Leu, Val
Leu	Ile, Val

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Original Residue	Exemplur: Substitutions
Lys	Arg, Gln, Glu
Met	Leu, Ile,
Phe	Met, Leu, Tyr
Ser	Thr
Thr	Ser
Ттр	Туг
Tyr	Trp, Phe
Val .	Ile, Leu

Conserved or non-conserved differences may correspond to polymorphisms in corresponding parent polypeptides. Polymorphic polypeptides are expressed by various pathogenic organisms and cancers. For example, the polymorphic polypeptides may be expressed by different viral strains or clades or by cancers in different individuals.

Sequence overlap between respective segments is preferable to minimise destruction of any epitope sequences that may result from any shuffling or rearrangement of the segments relative to their existing order in the parent polypeptide. If overlapping segments as described above are employed to form a synthetic polypeptide, it may not be necessary to change the order in which those segments are linked together relative to the order in which corresponding segments are normally present in the parent polypeptide. In this regard, such overlapping segments when linked together in the synthetic polypeptide can adopt a different structure relative to the structure of the parent polypeptide, wherein the different structure does not provide for one or more functions associated with the parent polypeptide. For example, in the case of four segments A-B-C-D each spanning 30 contiguous amino acids of the parent polypeptide and having a 10-amino acid overlapping sequence with one or more adjacent segments, the synthetic polypeptide will have duplicated 10-amino acid sequences bridging segments A-B, B-C and C-D. The presence of these duplicated sequences may be sufficient to render a different structure and to abrogate or alter function relative to the parent polypeptide.

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In a preferred embodiment, segment size is about 30 amino acids and sequence overlap at one or both ends of a respective segment is about 15 amino acids. However, it will be understood that other suitable segment sizes and sequence overlap sizes are contemplated by the present invention, which can be readily ascertained by persons of skill in the art.

It is preferable but not necessary to utilise all the segments of the parent polypeptide in the construction of the synthetic polypeptide. Suitably, at least 30%, preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, even more preferably at least 70%, even more preferably at least 80% and still even more preferably at least 90% of the parent polypeptide sequence is used in the construction of the synthetic polypeptide. However, it will be understood that the more sequence information from a parent polypeptide that is utilised to construct the synthetic polypeptide, the greater the population coverage will be of the synthetic polypeptide as an immunogen. Preferably, no sequence information from the parent polypeptide is excluded (e.g., because of an apparent lack of immunological epitopes).

Persons of skill in the art will appreciate that when preparing a synthetic polypeptide against a pathogenic organism (e.g., a virus) or a cancer, it may be preferable to use sequence information from a plurality of different polypeptides expressed by the organism or the cancer. Accordingly, in a preferred embodiment, segments from a plurality of different polypeptides are linked together to form a synthetic polypeptide according to the invention. It is preferable in this respect to utilise as many parent polypeptides as possible from, or in relation to, a particular source in the construction of the synthetic polypeptide. The source of parent polypeptides includes, but is not limited to, a pathogenic organism and a cancer. Suitably, at least about 30%, preferably at least 40%, more preferably at least 50%, even more preferably at least 60%, even more preferably at least 70%, even more preferably at least 80% and still even more preferably at least 90% of the parent polypeptides expressed by the source is used in the construction of the synthetic polypeptide. Preferably, parent polypeptides from a virus include, but are not restricted to. latent polypeptides, regulatory polypeptides or polypeptides expressed early during their replication cycle. Suitably, parent polypeptides from a parasite or bacterium include, but are not restricted to, secretory polypeptides and polypeptides expressed on the surface of

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the parasite or bacteria. It is preferred that parent polypeptides from a cancer or tumour are cancer specific polypeptides.

Suitably, hypervariable sequences within the parent polypeptide are excluded from the construction of the synthetic polypeptide.

The synthetic polypeptides of the inventions may be prepared by any suitable procedure known to those of skill in the art. For example, the polypeptide may be synthesised using solution synthesis or solid phase synthesis as described, for example, in Chapter 9 of Atherton and Shephard (1989, Solid Phase Peptide Synthesis: A Practical Approach. IRL Press, Oxford) and in Roberge et al (1995, Science 269: 202). Syntheses employ, t-butyloxycarbonyl for example, either may (t-Boc) 9fluorenylmethyloxycarbonyl (Fmoc) chemistries (see Chapter 9.1, of Coligan et al., CURRENT PROTOCOLS IN PROTEIN SCIENCE, John Wiley & Sons, Inc. 1995-1997: Stewart and Young, 1984, Solid Phase Peptide Synthesis, 2nd ed. Pierce Chemical Co., Rockford, Ill; and Atherton and Shephard, supra).

Alternatively, the polypeptides may be prepared by a procedure including the steps of:

- (a) preparing a synthetic construct including a synthetic polynucleotide encoding a synthetic polypeptide wherein said synthetic polynucleotide is operably linked to a regulatory polynucleotide, wherein said synthetic polypeptide comprises a plurality of different segments of a parent polypeptide, wherein said segments are linked together in a different relationship relative to their linkage in the parent polypeptide:
  - (b) introducing the synthetic construct into a suitable host cell;
- (c) culturing the host cell to express the synthetic polypeptide from said synthetic construct; and
- (d) isolating the synthetic polypeptide.

The synthetic construct is preferably in the form of an expression vector. For example, the expression vector can be a self-replicating extra-chromosomal vector such as a plasmid, or a vector that integrates into a host genome. Typically, the regulatory polynucleotide may include, but is not limited to, promoter sequences, leader or signal

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sequences, ribosomal binding sites, transcriptional start and stop sequences, translational start and termination sequences, and enhancer or activator sequences. Constitutive or inducible promoters as known in the art are contemplated by the invention. The promoters may be either naturally occurring promoters, or hybrid promoters that combine elements of more than one promoter. The regulatory polynucleotide will generally be appropriate for the host cell used for expression. Numerous types of appropriate expression vectors and suitable regulatory polynucleotides are known in the art for a variety of host cells.

In a preferred embodiment, the expression vector contains a selectable marker gene to allow the selection of transformed host cells. Selection genes are well known in the art and will vary with the host cell used.

The expression vector may also include a fusion partner (typically provided by the expression vector) so that the synthetic polypeptide of the invention is expressed as a fusion polypeptide with said fusion partner. The main advantage of fusion partners is that they assist identification and/or purification of said fusion polypeptide. In order to express said fusion polypeptide, it is necessary to ligate a polynucleotide according to the invention into the expression vector so that the translational reading frames of the fusion partner and the polynucleotide coincide.

Well known examples of fusion partners include, but are not limited to, glutathione-S-transferase (GST), Fc portion of human IgG, maltose binding protein (MBP) and hexahistidine (HIS6), which are particularly useful for isolation of the fusion polypeptide by affinity chromatography. For the purposes of fusion polypeptide purification by affinity chromatography, relevant matrices for affinity chromatography are glutathione-, amylose-, and nickel- or cobalt-conjugated resins respectively. Many such matrices are available in "kit" form, such as the QIAexpress<sup>TM</sup> system (Qiagen) useful with (HIS6) fusion partners and the Pharmacia GST purification system. In a preferred embodiment, the recombinant polynucleotide is expressed in the commercial vector pFLAG<sup>TM</sup>.

Another fusion partner well known in the art is green fluorescent protein (GFP). This fusion partner serves as a fluorescent "tag" which allows the fusion polypeptide of the invention to be identified by fluorescence microscopy or by flow cytometry. The GFP tag is useful when assessing subcellular localisation of a fusion polypeptide of the invention,

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or for isolating cells which express a fusion polypeptide of the invention. Flow cytometric methods such as fluorescence activated cell sorting (FACS) are particularly useful in this latter application. Preferably, the fusion partners also have protease cleavage sites, such as for Factor Xa, Thrombin and inteins (protein introns), which allow the relevant protease to partially digest the fusion polypeptide of the invention and thereby liberate the recombinant polypeptide of the invention therefrom. The liberated polypeptide can then be isolated from the fusion partner by subsequent chromatographic separation. Fusion partners according to the invention also include within their scope "epitope tags", which are usually short peptide sequences for which a specific antibody is available. Well known examples of epitope tags for which specific monoclonal antibodies are readily available include c-Myc, influenza virus, haemagglutinin and FLAG tags. Alternatively, a fusion partner may be provided to promote other forms of immunity. For example, the fusion partner may be an antigen-binding molecule that is immuno-interactive with a conformational epitope on a target antigen or to a post-translational modification of a target antigen (e.g., an antigen-binding molecule that is immuno-interactive with a glycosylated target antigen).

The step of introducing the synthetic construct into the host cell may be effected by any suitable method including transfection, and transformation, the choice of which will be dependent on the host cell employed. Such methods are well known to those of skill in the art.

Synthetic polypeptides of the invention may be produced by culturing a host cell transformed with the synthetic construct. The conditions appropriate for protein expression will vary with the choice of expression vector and the host cell. This is easily ascertained by one skilled in the art through routine experimentation.

Suitable host cells for expression may be prokaryotic or eukaryotic. One preferred host cell for expression of a polypeptide according to the invention is a bacterium. The bacterium used may be *Escherichia coli*. Alternatively, the host cell may be an insect cell such as, for example, *SF9* cells that may be utilised with a baculovirus expression system.

The synthetic polypeptide may be conveniently prepared by a person skilled in the art using standard protocols as for example described in Sambrook, et al., MOLECULAR CLONING. A LABORATORY MANUAL (Cold Spring Harbor Press, 1989), in particular

Sections 16 and 17; Ausubel et al., CURRENT PROTOCOLS IN MOLECULAR BIOLOGY (John Wiley & Sons, Inc. 1994-1998), in particular Chapters 10 and 16; and Coligan et al., CURRENT PROTOCOLS IN PROTEIN SCIENCE (John Wiley & Sons, Inc. 1995-1997), in particular Chapters 1, 5 and 6.

The amino acids of the synthetic polypeptide can be any non-naturally occurring or any naturally occurring amino acid. Examples of unnatural amino acids and derivatives during peptide synthesis include but are not limited to, use of 4-amino butyric acid, 6-aminohexanoic acid, 4-amino-3-hydroxy-5-phenylpentanoic acid, 4-amino-3-hydroxy-6-methylheptanoic acid, t-butylglycine, norleucine, norvaline, phenylglycine, ornithine, sarcosine, 2-thienyl alanine and/or D-isomers of amino acids. A list of unnatural amino acids contemplated by the present invention is shown in TABLE C.

TABLE C

Non-conventional animo acid	New-conventional amino setal
α-aminobutyric acid	L-N-methylalanine
α-amino-α-methylbutyrate	L-N-methylarginine
aminocyclopropane-carboxylate	L-N-methylasparagine
aminoisobutyric acid	L-N-methylaspartic acid
aminonorbornyl-carboxylate	L-N-methylcysteine
cyclohexylalanine	L-N-methylglutamine
cyclopentylalanine	L-N-methylglutamic acid
L-N-methylisoleucine	L-N-methylhistidine
D-alanine	L-N-methylleucine
D-arginine	L-N-methyllysine
D-aspartic acid	L-N-methylmethionine
D-cysteine	L-N-methylnorleucine
D-glutamate	L-N-methylnorvaline
D-glutamic acid	L-N-methylomithine

Non-conventional ampre acid	Non-conventional amino acid
D-histidine	L-N-methylphenylalanine
D-isoleucine	L-N-methylproline
D-leucine	L-N-medlylserine
D-lysine	
D-nethionine	L-N-methylthreonine
	L-N-methyltryptophan
D-ornithine	L-N-methyltyrosine
D-phenylalanine	L-N-methylvaline
D-proline	L-N-methylethylglycine
D-serine	L-N-methyl-t-butylglycine
D-threonine	L-norleucine
D-tryptophan	L-norvaline
D-tyrosine	α-methyl-aminoisobutyrate
D-valine	α-methyl-γ-aminobutyrate
D-α-methylalanine	α-methylcyclohexylalanine
D-α-methylarginine	α-methylcylcopentylalanine
D-α-methylasparagine	α-methyl-α-napthylalanine
D-0-methylaspartate	α-methylpenicillamine
D-a-methylcysteine	N-(4-aminobutyl)glycine
D-α-methylglutamine	N-(2-aminoethyl)glycine
D-α-methylhistidine	N-(3-aminopropyl)glycine
D-α-methylisoleucine	N-amino-α-methylbutyrate
D-α-methylleucine	α-napthylalanine
D-a-methyllysine	N-benzylglycine
D-α-methylmethionine	N-(2-carbamylediyl)glycine
D-\a-methylornithiine	N-(carbamylmethyl)glycine

Non-conventional amino add	Non-communicated curitio acid
D-α-methylphenylalanine	N-(2-carboxyethyl)glycine
D-α-methylproline	N-(carboxymethyl)glycine
D-α-methylserine	N-cyclobutylglycine
D-α-methylthreonine	N-cycloheptylglycine
D-α-methyltryptophan	N-cyclohexylglycine
D-α-methyltyrosine	N-cyclodecylglycine
L-\a-methylleucine	L-\alpha-methyllysine
L-a-methylmethionine	L-α-methylnorleucine
L-a-methylnorvatine	L-α-methylornithine
L-α-methylphenylalanine	L-a-methylproline
L-α-methylserine	L-\alpha-methylthreonine
L-α-methyltryptophan	L-\a-methyltyrosine
L-α-methylvaline	L-N-methylhomophenylalanine
N-(N-(2,2-diphenylethyl carbamylmethyl)glycine	N-(N-(3,3-diphenylpropyl carbamylmethyl)glycine
1-carboxy-1-(2,2-diphenyl-ethyl amino)cyclopropane	

The invention also contemplates modifying the synthetic polypeptides of the invention using ordinary molecular biological techniques so as to alter their resistance to proteolytic degradation or to optimise solubility properties or to render them more suitable as an immunogenic agent.

## 3. Preparation of synthetic polynucleotides of the invention

The invention contemplates synthetic polynucleotides encoding the synthetic polypeptides as for example described in Section 2 supra. Polynucleotides encoding segments of a parent polypeptide can be produced by any suitable technique. For example, such polynucleotides can be synthesised de novo using readily available machinery.

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Sequential synthesis of DNA is described, for example, in U.S. Patent No 4,293,652. Instead of *de novo* synthesis, recombinant techniques may be employed including use of restriction endonucleases to cleave a polynucleotide encoding at least a segment of the parent polypeptide and use of ligases to ligate together in frame a plurality of cleaved polynucleotides encoding different segments of the parent polypeptide. Suitable recombinant techniques are described for example in the relevant sections of Ausubel, *et al.* (*supra*) and of Sambrook, *et al.*, (*supra*) which are incorporated herein by reference. Preferably, the synthetic polynucleotide is constructed using splicing by overlapping extension (SOEing) as for example described by Horton *et al.* (1990, *Biotechniques* 8(5): 528-535; 1995, *Mol Biotechnol.* 3(2): 93-99; and 1997, *Methods Mol Biol.* 67: 141-149). However, it should be noted that the present invention is not dependent on, and not directed to, any one particular technique for constructing the synthetic construct.

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Various modifications to the synthetic polynucleotides may be introduced as a means of increasing intracellular stability and half-life. Possible modifications include but are not limited to the addition of flanking sequences of ribo- or deoxy- nucleotides to the 5' and/or 3' ends of the molecule or the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages within the oligodeoxyribonucleotide backbone.

The invention therefore contemplates a method of producing a synthetic polynucleotide as broadly described above, comprising linking together in the same reading frame at least two nucleic acid sequences encoding different segments of a parent polypeptide to form a synthetic polynucleotide, which encodes a synthetic polypeptide according to the invention. Suitably, nucleic acid sequences encoding at least 10 segments, preferably at least 20 segments, more preferably at least 40 segments and more preferably at least 100 segments of a parent polypeptide are employed to produce the synthetic polynucleotide.

Preferably, the method further comprises selecting segments of the parent polypeptide, reverse translating the selected segments and preparing nucleic acid sequences encoding the selected segments. It is preferred that the method further comprises randomly linking the nucleic acid sequences together to form the synthetic polynucleotide. The nucleic acid sequences may be oligonucleotides or polynucleotides.

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Suitably, segments are selected on the basis of size. Additionally, or in the alternative, segments are selected such that they have partial sequence identity or homology (i.e., sequence overlap) with one or more other segments. A number of factors can influence segment size and sequence overlap as mentioned above. In the case of sequence overlap, large amounts of duplicated nucleic acid sequences can sometimes result in sections of nucleic acid being lost during nucleic acid amplification (e.g., polymerase chain reaction, PCR) of such sequences, recombinant plasmid propagation in a bacterial host or during amplification of recombinant viruses containing such sequences. Accordingly, in a preferred embodiment, nucleic acid sequences encoding segments having sequence identity or homology with one or more other encoded segments are not linked together in an arrangement in which the identical or homologous sequences are contiguous. Also, it is preferable that different codons are used to encode a specific amino acid in a duplicated region. In this context, an amino acid of a parent polypeptide sequence is preferably reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence (e.g., a duplicated sequence or a palindromic sequence) that is refractory to the execution of a task (e.g., cloning or sequencing). Alternatively, segments may be selected such that they contain a carboxyl terminal leucine residue or such that reverse translated sequences encoding the segments contain restriction enzyme sites for convenient splicing of the reverse translated sequences.

The method optionally further comprises linking a spacer oligonucleotide encoding at least one spacer residue between segment-encoding nucleic acids. Such spacer residue(s) may be advantageous in ensuring that epitopes within the segments are processed and presented efficiently. Preferably, the spacer oligonucleotide encodes 2 to 3 spacer residues. The spacer residue is suitably a neutral amino acid, which is preferably alanine.

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Optionally, the method further comprises linking in the same reading frame as other segment-containing nucleic acid sequences at least one variant nucleic acid sequence which encodes a variant segment having a homologous but not identical amino acid sequence relative to other encoded segments. Suitably, the variant segment comprises conserved and/or non-conserved amino acid differences relative to one or more other encoded segments. Such differences may correspond to polymorphisms as discussed

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above. In a preferred embodiment, degenerate bases are designed or built in to the at least one variant nucleic acid sequence to give rise to all desired homologous sequences.

When a large number of polymorphisms is intended to be covered, it is preferred that multiple synthetic polynucleotides are constructed rather than a single synthetic polynucleotide, which encodes all variant segments. For example, if there is less than 85% homology between polymorphic polypeptides, then it is preferred that more than one synthetic polynucleotide is constructed.

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Preferably, the method further comprises optimising the codon composition of the synthetic polynucleotide such that it is translated efficiently by a host cell. In this regard, it is well known that the translational efficiency of different codons varies between organisms and that such differences in codon usage can be utilised to enhance the level of protein expression in a particular organism. In this regard, reference may be made to Seed et al. (International Application Publication No WO 96/09378) who disclose the replacement of existing codons in a parent polynucleotide with synonymous codons to enhance expression of viral polypeptides in mammalian host cells. Preferably, the first or second most frequently used codons are employed for codon optimisation.

Preferably, gene splicing by overlap extension or "gene SOEing" (supra) is employed for the construction of the synthetic polynucleotide which is a PCR-based method of recombining DNA sequences without reliance on restriction sites and of directly generating mutated DNA fragments in vitro. By modifying the sequences incorporated into the 5'-ends of the primers, any pair of PCR products can be made to share a common sequence at one end. Under PCR conditions, the common sequence allows strands from two different fragments to hybridise to one another, forming an overlap. Extension of this overlap by DNA polymerase yields a recombinant molecule. However, a problem with long synthetic constructs is that mutations generally incorporate into amplified products during synthesis. In this instance, it is preferred that resolvase treatment is employed at various steps of the synthesis. Resolvases are bacteriophage-encoded endonucleases which recognise disruptions or mispairing of double stranded DNA and are primarily used by bacteriophages to resolve Holliday junctions (Mizuuchi, 1982; Youil et al., 1995). For example, T7 endonuclease I can be employed in synthetic DNA constructions to recognise mutations and cleave corrupted dsDNA. The mutated DNA strands are then hybridised to

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non-mutant or correct DNA sequences, which results in a mispairing of DNA bases. The mispaired bases are recognised by the resolvase, which then cleaves the DNA nearby leaving only correctly hybridised sequences intact. Preferably a thermostable resolvase enzyme is employed during splicing or amplification so that errors are not incorporated in downstream synthesis products.

Synthetic polynucleotides according to the invention can be operably linked to a regulatory polynucleotide in the form a synthetic construct as for example described in Section 2 supra. Synthetic constructs of the invention have utility inter alia as nucleic acid vaccines. The choice of regulatory polynucleotide and synthetic construct will depend on the intended host.

Exemplary expression vectors for expression of a synthetic polypeptide according to the invention include, but are not restricted to, modified Ankara Vaccinia virus as for example described by Allen et al. (2000, J. Immunol. 164(9): 4968-4978), fowlpox virus as for example described by Boyle and Coupar (1988, Virus Res. 10: 343-356) and the herpes simplex amplicons described for example by Fong et al. in U.S. Patent No. 6,051,428. Alternatively, Adenovirus and Epstein-Barr virus vectors, which are preferably capable of accepting large amounts of DNA or RNA sequence information, can be used.

Preferred promoter sequences that can be utilised for expression of synthetic polypeptides include the P7.5 or PE/L promoters as for example disclosed by Kumar and 20 Boyle. (1990, Virology 179: 151-158), CMV and RSV promoters.

The synthetic construct optionally further includes a nucleic acid sequence encoding an immunostimulatory molecule. The immunostimulatory molecule may be fusion partner of the synthetic polypeptide. Alternatively, the immunostimulatory molecule may be translated separately from the synthetic polypeptide. Preferably, the immunostimulatory molecule comprises a general immunostimulatory peptide sequence. For example, the immunostimulatory peptide sequence may comprise a domain of an invasin protein (Inv) from the bacteria Yersinia spp as for example disclosed by Brett et al. (1993, Eur. J. Immunol. 23: 1608-1614). This immune stimulatory property results from the capability of this invasin domain to interact with the β1 integrin molecules present on T cells, particularly activated immune or memory T cells. A preferred embodiment of the invasin domain (Inv) for linkage to a synthetic polypeptide has been previously described

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in U.S. Pat. No. 5,759,551. The said Inv domain has the sequence: Thr-Ala-Lys-Ser-Lys-Lys-Phe-Pro-Ser-Tyr-Thr-Ala-Thr-Tyr-Gln-Phe [SEQ ID NO; 1467] or is an immune stimulatory homologue thereof from the corresponding region in another Yersinia species invasin protein. Such homologues thus may contain substitutions, deletions or insertions of amino acid residues to accommodate strain to strain variation, provided that the homologues retain immune stimulatory properties. The general immunostimulatory sequence may optionally be linked to the synthetic polypeptide by a spacer sequence.

In an alternate embodiment, the immunostimulatory molecule may comprise an immunostimulatory membrane or soluble molecule, which is suitably a T cell costimulatory molecule. Preferably, the T cell co-stimulatory molecule is a B7 molecule or a biologically active fragment thereof, or a variant or derivative of these. The B7 molecule includes, but is not restricted to, B7-1 and B7-2. Preferably, the B7 molecule is B7-1. Alternatively, the T cell co-stimulatory molecule may be an ICAM molecule such as ICAM-1 and ICAM-2.

In another embodiment, the immunostimulatory molecule can be a cytokine. which includes, but is not restricted to, an interleukin, a lymphokine, tumour necrosis factor and an interferon. Alternatively, the immunostimulatory molecule may comprise an immunomodulatory oligonucleotide as for example disclosed by Krieg in U.S. Patent No. 6,008,200.

Suitably, the size of the synthetic polynucleotide does not exceed the ability of host cells to transcribe, translate or proteolytically process and present epitopes to the immune system. Practitioners in the art will also recognise that the size of the synthetic polynucleotide can impact on the capacity of an expression vector to express the synthetic polynucleotide in a host cell. In this connection, it is known that the efficacy of DNA 25 vaccination reduces with expression vectors greater that 20-kb. In such situations it is preferred that a larger number of smaller synthetic constructs is utilised rather than a single large synthetic construct.

#### 4. Immunopotentiating compositions

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invention also contemplates a composition, comprising 30 immunopotentiating agent selected from the group consisting of a synthetic polypeptide as

described in Section 2, and a synthetic polynucleotide or a synthetic construct as described in Section 3, together with a pharmaceutically acceptable carrier. One or more immunopotentiating agents can be used as actives in the preparation of immunopotentiating compositions. Such preparation uses routine methods known to persons skilled in the art. Typically, such compositions are prepared as injectables, either as liquid solutions or suspensions; solid forms suitable for solution in, or suspension in, liquid prior to injection may also be prepared. The preparation may also be emulsified. The active immunogenic ingredients are often mixed with excipients that are pharmaceutically acceptable and compatible with the active ingredient. Suitable excipients are, for example, water, saline, dextrose, glycerol, ethanol, or the like and combinations thereof. In addition, if desired, the vaccine may contain minor amounts of auxiliary substances such as wetting or emulsifying agents, pH buffering agents, and/or adjuvants that enhance the effectiveness of the vaccine. Examples of adjuvants which may be effective include but are not limited to: aluminium hydroxide, N-acetyl-muramyl-L-threonyl-D-isoglutamine (thur-MDP), Nacetyl-nor-muramyl-L-alanyl-D-isoglutamine (CGP 11637, referred to as nor-MDP), Nacetylmuramyl-L-alanyl-D-isoglutaminyl-L-alanine-2-(1'-2'-dipalmitoyl-sn-glycero-3hydroxyphosphoryloxy)-ethylamine (CGP 1983A, referred to as MTP-PE), and RIBI, which contains three components extracted from bacteria, monophosphoryl lipid A, trehalose dimycolate and cell wall skeleton (MPL+TDM+CWS) in a 2% squalene/Tween 80 emulsion. For example, the effectiveness of an adjuvant may be determined by measuring the amount of antibodies resulting from the administration of the composition, wherein those antibodies are directed against one or more antigens presented by the treated cells of the composition.

The immunopotentiating agents may be formulated into a composition as neutral or salt forms. Pharmaceutically acceptable salts include the acid addition salts (formed with free amino groups of the peptide) and which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids such as acetic, oxalic, tartaric, maleic, and the like. Salts formed with the free carboxyl groups may also be derived from inorganic basis such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic basis as isopropylamine, trimethylamine, 2-ethylamino ethanol, histidine, procaine, and the like.

If desired, devices or compositions containing the immunopotentiating agents suitable for sustained or intermittent release could be, in effect, implanted in the body or topically applied thereto for the relatively slow release of such materials into the body.

The compositions are conventionally administered parenterally, by injection, for example, either subcutaneously or intramuscularly. Additional formulations which are suitable for other modes of administration include suppositories and, in some cases, oral formulations. For suppositories, traditional binders and carriers may include, for example, polyalkylene glycols or triglycerides; such suppositories may be formed from mixtures containing the active ingredient in the range of 0.5% to 10%, preferably 1%-2%. Oral formulations include such normally employed excipients as, for example, pharmaceutical grades of mannitol, lactose, starch, magnesium carbonate, and the like. These compositions take the form of solutions, suspensions, tablets, pills, capsules, sustained release formulations or powders and contain 10%-95% of active ingredient, preferably 25%-70%.

Administration of the gene therapy construct to said mammal, preferably a human, may include delivery via direct oral intake, systemic injection, or delivery to selected tissue(s) or cells, or indirectly via delivery to cells isolated from the mammal or a compatible donor. An example of the latter approach would be stem cell therapy, wherein isolated stem cells having potential for growth and differentiation are transfected with the vector comprising the *Sox18* nucleic acid. The stem cells are cultured for a period and then transferred to the mammal being treated.

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With regard to nucleic acid based compositions, all modes of delivery of such compositions are contemplated by the present invention. Delivery of these compositions to cells or tissues of an animal may be facilitated by microprojectile bombardment, liposome mediated transfection (e.g., lipofectin or lipofectamine), electroporation, calcium phosphate or DEAE-dextran-mediated transfection, for example. In an alternate embodiment, a synthetic construct may be used as a therapeutic or prophylactic composition in the form of a "naked DNA" composition as is known in the art. A discussion of suitable delivery methods may be found in Chapter 9 of CURRENT PROTOCOLS IN MOLECULAR BIOLOGY (Eds. Ausubel et al.; John Wiley & Sons Inc., 1997 Edition) or on the Internet site DNAvaccine.com. The compositions may be administered by intradermal (e.g., using panjet<sup>TM</sup> delivery) or intramuscular routes.

The step of introducing the synthetic polynucleotide into a target cell will differ depending on the intended use and species, and can involve one or more of non-viral and viral vectors, cationic liposomes, retroviruses, and adenoviruses such as, for example, described in Mulligan, R.C., (1993 *Science* 260 926-932) which is hereby incorporated by reference. Such methods can include, for example:

A. Local application of the synthetic polynucleotide by injection (Wolff et al., 1990, Science 247 1465-1468, which is hereby incorporated by reference), surgical implantation, instillation or any other means. This method can also be used in combination with local application by injection, surgical implantation, instillation or any other means, of cells responsive to the protein encoded by the synthetic polynucleotide so as to increase the effectiveness of that treatment. This method can also be used in combination with local application by injection, surgical implantation, instillation or any other means, of another factor or factors required for the activity of said protein.

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- B. General systemic delivery by injection of DNA, (Calabretta et al., 1993, Cancer Treat. Rev. 19 169-179, which is incorporated herein by reference), or RNA, alone or in combination with liposomes (Zhu et al., 1993, Science 261 209-212, which is incorporated herein by reference), viral capsids or nanoparticles (Bertling et al., 1991, Biotech. Appl. Biochem. 13 390-405, which is incorporated herein by reference) or any other mediator of delivery. Improved targeting might be achieved by linking the synthetic polynucleotide to a targeting molecule (the so-called "magic bullet" approach employing, for example, an antibody), or by local application by injection, surgical implantation or any other means, of another factor or factors required for the activity of the protein encoding said synthetic polynucleotide, or of cells responsive to said protein.
  - C. Injection or implantation or delivery by any means, of cells that have been modified ex vivo by transfection (for example, in the presence of calcium phosphate: Chen et al., 1987, Mole. Cell Biochem. 7 2745-2752, or of cationic lipids and polyamines: Rose et al., 1991, BioTech. 10 520-525, which articles are incorporated herein by reference), infection, injection, electroporation (Shigekawa et al., 1988, BioTech. 6 742-751, which is incorporated herein by reference) or any other way so as to increase the

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expression of said synthetic polynucleotide in those cells. The modification can be mediated by plasmid, bacteriophage, cosmid, viral (such as adenoviral or retroviral; Mulligan, 1993, Science 260 926-932; Miller, 1992, Nature 357 455-460; Salmons et al., 1993, Hum. Gen. Ther. 4 129-141, which articles are incorporated herein by reference) or other vectors, or other agents of modification such as liposomes (Zhu et al., 1993, Science 261 209-212, which is incorporated herein by reference), viral capsids or nanoparticles (Bertling et al., 1991, Biotech. Appl. Biochem. 13 390-405, which is incorporated herein by reference), or any other mediator of modification. The use of cells as a delivery vehicle for genes or gene products has been described by Barr et al., 1991, Science 254 1507-1512 and by Dhawan et al., 1991, Science 254 1509-1512, which articles are incorporated herein by reference. Treated cells can be delivered in combination with any nutrient, growth factor, matrix or other agent that will promote their survival in the treated subject.

Also encapsulated by the present invention is a method for treatment and/or prophylaxis of a disease or condition, comprising administering to a patient in need of such treatment a therapeutically effective amount of a composition as broadly described above. The disease or condition may be caused by a pathogenic organism or a cancer as for example described above.

In a preferred embodiment, the immunopotentiating composition of the invention is suitable for treatment of, or prophylaxis against, a cancer. Cancers which could be suitably treated in accordance with the practices of this invention include cancers of the lung, breast, ovary, cervix, colon, head and neck, pancreas, prostate, stomach, bladder, kidney, bone liver, oesophagus, brain, testicle, uterus, melanoma and the various leukemias and lymphomas.

In an alternate embodiment, the immunopotentiating composition is suitable for treatment of, or prophylaxis against, a viral, bacterial or parasitic infection. Viral infections contemplated by the present invention include, but are not restricted to, infections caused by HIV, Hepatitis, Influenza, Japanese encephalitis virus, Epstein-Barr virus and respiratory syncytial virus. Bacterial infections include, but are not restricted to, those caused by Neisseria species, Meningococcal species, Haemophilus species Salmonella species, Streptococcal species, Legionella species and Mycobacterium species. Parasitic

infections encompassed by the invention include, but are not restricted to, those caused by *Plasmodium* species, *Schistosoma* species, *Leishmania* species, *Trypanosoma* species, *Toxoplasma* species and *Giardia* species.

The above compositions or vaccines may be administered in a manner compatible

with the dosage formulation, and in such amount as is therapeutically effective to alleviate
patients from the disease or condition or as is prophylactically effective to prevent
incidence of the disease or condition in the patient. The dose administered to a patient, in
the context of the present invention, should be sufficient to effect a beneficial response in a
patient over time such as a reduction or cessation of blood loss. The quantity of the
composition or vaccine to be administered may depend on the subject to be treated
inclusive of the age, sex, weight and general health condition thereof. In this regard,
precise amounts of the composition or vaccine for administration will depend on the
judgement of the practitioner. In determining the effective amount of the composition or
vaccine to be administered in the treatment of a disease or condition, the physician may
evaluate the progression of the disease or condition over time. In any event, those of skill
in the art may readily determine suitable dosages of the composition or vaccine of the
invention.

In a preferred embodiment, DNA-based immunopotentiating agent (e.g., 100  $\mu$ g) is delivered intradermally into a patient at day 1 and at week 8 to prime the patient. A recombinant poxvirus (e.g., at  $10^7$  pfu/mL) from which substantially the same immunopotentiating agent can be expressed is then delivered intradermally as a booster at weeks 16 and 24, respectively.

The effectiveness of the immunisation may be assessed using any suitable technique. For example, CTL lysis assays may be employed using stimulated splenocytes or peripheral blood mononuclear cells (PBMC) on peptide coated or recombinant virus infected cells using <sup>51</sup>Cr labelled target cells. Such assays can be performed using for example primate, mouse or human cells (Allen et al., 2000, J. Immunol. 164(9): 4968-4978 also Woodberry et al., infra). Alternatively, the efficacy of the immunisation may be monitored using one or more techniques including, but not limited to, HLA class I Tetramer staining - of both fresh and stimulated PBMCs (see for example Allen et al., supra), proliferation assays (Allen et al., supra), Elispot<sup>TM</sup> Assays and intracellular INF-

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gamma staining (Allen et al., supra), ELISA Assays - for linear B cell responses; and Western blots of cell sample expressing the synthetic polynucleotides.

## 5. Computer related embodiments

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The design or construction of a synthetic polypeptide sequence or a synthetic polynucleotide sequence according to the invention is suitably facilitated with the assistance of a computer programmed with software, which inter alia fragments a parent sequence into fragments, and which links those fragments together in a different relationship relative to their linkage in the parent sequence. The ready use of a parent sequence for the construction of a desired synthetic molecule according to the invention requires that it be stored in a computer-readable format. Thus, in accordance with the present invention, sequence data relating to a parent molecule (e.g., a parent polypeptide) is stored in a machine-readable storage medium, which is capable of processing the data to fragment the sequence of the parent molecule into fragments and to link together the fragments in a different relationship relative to their linkage in the parent molecule.

Therefore, another embodiment of the present invention provides a machinereadable data storage medium, comprising a data storage material encoded with machine readable data which, when used by a machine programmed with instructions for using said data, fragments a parent sequence into fragments, and links those fragments together in a different relationship relative to their linkage in the parent sequence. In a preferred 20 embodiment of this type, a machine-readable data storage medium is provided that is capable of reverse translating the sequence of a respective fragment to provide a nucleic acid sequence encoding the fragment and to link together in the same reading frame each of the nucleic acid sequences to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship 25 relative to their linkage in a parent polypeptide sequence.

In another embodiment, the invention encompasses a computer for designing the sequence of a synthetic polypeptide and/or a synthetic polynucleotide of the invention. wherein the computer comprises wherein said computer comprises: (a) a machine readable data storage medium comprising a data storage material encoded with machine readable data, wherein said machine readable data comprises the sequence of a parent polypeptide; (b) a working memory for storing instructions for processing said machine-readable data;

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(c) a central-processing unit coupled to said working memory and to said machine-readable data storage medium, for processing said machine-readable data into said synthetic polypeptide sequence and/or said synthetic polynucleotide; and (d) an output hardware coupled to said central processing unit, for receiving said synthetic polypeptide sequence and/or said synthetic polynucleotide.

In yet another embodiment, the invention contemplates a computer program product for designing the sequence of a synthetic polynucleotide of the invention, comprising code that receives as input the sequence of a parent polypeptide, code that fragments the sequence of the parent polypeptide into fragments, code that reverse translates the sequence of a respective fragment to provide a nucleic acid sequence encoding the fragment, code that links together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the parent polypeptide sequence, and a computer readable medium that stores the codes.

A version of these embodiments is presented in Figure 23, which shows a system 10 including a computer 11 comprising a central processing unit ("CPU") 20, a working memory 22 which may be, e.g., RAM (random-access memory) or "core" memory, mass storage memory 24 (such as one or more disk drives or CD-ROM drives), one or more cathode-ray tube ("CRT") display terminals 26, one or more keyboards 28, one or more input lines 30, and one or more output lines 40, all of which are interconnected by a conventional bidirectional system bus 50.

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Input hardware 36, coupled to computer 11 by input lines 30, may be implemented in a variety of ways. For example, machine-readable data of this invention 25 may be inputted via the use of a modern or moderns 32 connected by a telephone line or dedicated data line 34. Alternatively or additionally, the input hardware 36 may comprise CD. Alternatively, ROM drives or disk drives 24 in conjunction with display terminal 26, keyboard 28 may also be used as an input device.

Output hardware 46, coupled to computer 11 by output lines 40, may similarly be implemented by conventional devices. By way of example, output hardware 46 may include CRT display terminal 26 for displaying a synthetic polynucleotide sequence or a synthetic polypeptide sequence as described herein. Output hardware might also include a

printer 42, so that hard copy output may be produced, or a disk drive 24, to store system output for later use.

In operation, CPU 20 coordinates the use of the various input and output devices 36,46 coordinates data accesses from mass storage 24 and accesses to and from working memory 22, and determines the sequence of data processing steps. A number of programs may be used to process the machine readable data of this invention. Exemplary programs may use for example the steps outlined in the flow diagram illustrated in Figure 24. Broadly, these steps include (1) inputting at least one parent polypeptide sequence; (2) optionally adding to alanine spacers at the ends of each polypeptide sequence; (3) fragmenting the polypeptide sequences into fragments (e.g., 30 amino acids long), which are preferably overlapping (e.g., by 15 amino acids); (4) reverse translating the fragment to provide a nucleic acid sequence for each fragment and preferably using for the reverse translation first and second most translationally efficient codons for a cell type, wherein the codons are preferably alternated out of frame with each other in the overlaps of consecutive fragments; (5) randomly rearranging the fragments; (6) checking whether rearranged fragments recreate at least a portion of a parent polypeptide sequence; (7) repeating randomly rearranging the fragments when rearranged fragments recreate said at least a portion; or otherwise (8) linking the rearranged fragments together to produce a synthetic polypeptide sequence and/or a synthetic polynucleotide sequence; and (9) 20 outputting said synthetic polypeptide sequence and/or a synthetic polynucleotide sequence. An example of an algorithm which uses inter alia the aforementioned steps is shown in Figure 25. By way of example, this algorithm has been used for the design of synthetic polynucleotides and synthetic polypeptides according to the present invention for Hepatitis C 1a and for melanoma, as illustrated in Figures 26 and 27.

Figure 28 shows a cross section of a magnetic data storage medium 100 which can be encoded with machine readable data, or set of instructions, for designing a synthetic molecule of the invention, which can be carried out by a system such as system 10 of Figure 23. Medium 100 can be a conventional floppy diskette or hard disk, having a suitable substrate 101, which may be conventional, and a suitable coating 102, which may 30 be conventional, on one or both sides, containing magnetic domains (not visible) whose polarity or orientation can be altered magnetically. Medium 100 may also have an opening (not shown) for receiving the spindle of a disk drive or other data storage device 24. The

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magnetic domains of coating 102 of medium 100 are polarised or oriented so as to encode in manner which may be conventional, machine readable data such as that described herein, for execution by a system such as system 10 of Figure 23.

Figure 29 shows a cross section of an optically readable data storage medium 110 which also can be encoded with such a machine-readable data, or set of instructions, for designing a synthetic molecule of the invention, which can be carried out by a system such as system 10 of Figure 23. Medium 110 can be a conventional compact disk read only memory (CD-ROM) or a rewritable medium such as a magneto-optical disk, which is optically readable and magneto-optically writable. Medium 100 preferably has a suitable substrate 111, which may be conventional, and a suitable coating 112, which may be conventional, usually of one side of substrate 111.

In the case of CD-ROM, as is well known, coating 112 is reflective and is impressed with a plurality of pits 113 to encode the machine-readable data. The arrangement of pits is read by reflecting laser light off the surface of coating 112. A protective coating 114, which preferably is substantially transparent, is provided on top of coating 112.

In the case of a magneto-optical disk, as is well known, coating 112 has no pits 113, but has a plurality of magnetic domains whose polarity or orientation can be changed magnetically when heated above a certain temperature, as by a laser (not shown). The orientation of the domains can be read by measuring the polarisation of laser light reflected from coating 112. The arrangement of the domains encodes the data as described above.

In order that the invention may be readily understood and put into practical effect, particular preferred non-limiting embodiments will now be described as follows.

### **EXAMPLES**

## EXAMPLE 1

### Preparation of an HIV Savine

## **Experimental Protocol**

#### 5 Plasmids

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The plasmid pDNAVacc is ampicillin resistant and contains an expression cassette comprising a CMV promoter and enhancer, a synthetic intron, a multiple cloning site (MCS) and a SV40poly A signal sequence (Thomson *et al.*, 1998). The plasmid pTK7.5 and contains a selection cassette, a pox virus 7.5 early/late promoter and a MCS flanked on either side by Vaccinia virus TK gene sequences.

#### Recombinant Vaccinia Viruses

Recombinant Vaccinia viruses expressing the gag, env (IIB) and pol (LAI) genes of HIV-1 were used as previously described and denoted VV-GAG, VV-POL, VV-ENV (Woodberry et al., 1999; Kent et al., 1998).

### 15 Marker Rescue Recombination

Recombinant Vaccinia viruses containing Savine constructs were generated by marker rescue recombination, using protocols described previously (Boyle et al., 1985). Plaque purified viruses were tested for the TK phenotype and for the appropriate genome arrangement by Southern blot and PCR.

### 20 Oligonucleotides

Oligonucleotides 50 nmol scale and desalted were purchased from Life Technologies. Short oligonucleotides were resuspended in 100  $\mu$ L of water, their concentration determined, then diluted to 20  $\mu$ M for use in PCR or sequencing reactions. Long oligonucleotides for splicing reactions were denatured for 5 minutes at 94°C in 20  $\mu$ L of formamide loading buffer then 0.5  $\mu$ L gel purified on a 6% polyacrylamide gel.

Gel slices containing full-length oligonucleotides were visualised with ethidium bromide, excised, placed in Eppendorf<sup>TM</sup> tubes, combined with 200 μL of water before being crushed using the plunger of a 1 mL syringe. Before being used in splicing reactions the crushed gel was resuspended in an appropriate volume of buffer and 1-2 μL of the resuspendate used directly in the splicing reactions.

## Sequencing

Sequencing was performed using Dye terminator sequencing reactions and analyzed by the Biomedical Resource Facility at the John Curtin School of Medical Research using an ABI automated sequencer.

## 10 Restimulation of Lymphocytes from HIV Infected Patients

Two pools of recombinant Vaccinia viruses containing VV-AC1 + VV-BC1 (Pool 1) or VV-AC2 + VV-BC2 + VV-CC2 (Pool 2) were used to restimulate lymphocytes from the blood samples of HIV-infected patients. Briefly CTL lines were generated from HIV-infected donor PBMC. A fifth of the total PBMC were infected with either Pool 1 or Pool 2 Vaccinia viruses then added back to the original cell suspension. The infected cell suspension was then cultured with IL-7 for 1 week.

## CTL Assays

Restimulated PBMCs were used as effectors in a standard <sup>51</sup>Cr-release CTL assay. Targets were autologous EBV-transformed lymphoblastoid cell lines (LCLs) infected with the following viruses: Pool 1, Pool 2,VV-GAG, VV-POL or VV-ENV. Assay controls included uninfected targets, targets infected with VV-lacZ (virus control) and K562 cells.

#### Results

### HIV Savine Design

A main goal of the Savine strategy is to include as much protein sequence 25 information from a pathogen or cancer as possible in such a way that potential T cell epitopes remain intact and so that the vaccine or therapy is extremely safe. An HIV Savine is described herein not only to compare this strategy to other strategies but also, to produce

an HIV vaccine that would provide the maximum possible population coverage as well as catering for the major HIV clades.

A number of design criteria was first determined to exploit the many advantages of using a synthetic approach. One advantage is that it is possible to use consensus protein sequences to design these vaccines. Using consensus sequences for a highly variable virus like HIV should provide better vaccine coverage because individual viral isolate sequences may have lost epitopes which induce CTL against the majority of other viral isolates. Thus, using the consensus sequences of each HIV clade rather than individual isolate sequences should provide better vaccine coverage. Taking this one step further, a consensus sequence that covers all HIV clades should theoretically provide better coverage than using just the consensus sequences for individual clades. Before designing such a sequence however, it was decided that a more appropriate and focussed HIV vaccine might be constructed if the various clades were first ranked according to their relative importance. To establish such a ranking the following issues were considered, current prevalence of each clade, the rate at which each clade is increasing and the capacity of various regions of the world to cope with the HIV pandemic (Figures 1 and 2). These criteria produced the following ranking. Clade  $E \ge$  clade A > clade C > clade B > clade D > other clades. Clades E and A were considered to almost equal since they are very similar except in their envelope protein sequences, which differ considerably.

Another advantage of synthesising a designed sequence is that it is possible to incorporate degenerate sequences into their design. In the case of HIV, this means that more than one amino acid can be included at various positions to improve the ability of the vaccine to cater for the various HIV clades and isolates. Coverage is improved because mutations in different HIV clades and also in individual isolate sequences, while mostly destroying specific T cell epitopes, can result in the formation of new potentially useful epitopes nearby (Goulder et al., 1997). Incorporating degenerate amino acid sequences, however, also means that more than one construct must be made and mixed together. The number of constructs required depends on the frequency with which mutations are incorporated into the design. While this approach requires the construction of additional constructs, these constructs can be prepared from the same set of degenerate long oligonucleotides, significantly reducing the cost of providing such considerable interclade coverage.

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A set of degeneracy rules was developed for the incorporation of amino acid mutations into the design which meant that a maximum of eight constructs would be required so that theoretically all combinations were present, as follows: 1) Two amino acids at three positions (or less) within any group of nine amino acids (i.e., present in a CTL epitope); 2) Three amino acids at one position and two at another (or not) within any group of nine amino acids; 3) Four amino acids at one position and two at another (or not) within any group of nine amino acids. The reason why these rules were applied to nine amino acids (the average CTL epitope size) and not to larger stretches of amino acid sequence to cater for class II restricted epitopes, is because class II-restricted epitopes generally have a core sequence of nine amino acids in the middle which bind specifically to class II MHC molecules with the extra flanking sequences stabilising binding, by associating with either side of class II MHC antigens in a largely sequence independent manner (Brown et al., 1993).

Using the HIV clade ranking described above, the amino acid degeneracy rules and in some situations the similarity between amino acids, a degenerate consensus protein sequence was designed for each HIV protein using the consensus protein sequences for each HIV clade compiled by the Los Alamos HIV sequence database (Figures 3-11) (HIV Molecular Immunology Database, 1997). It is important to note that in some situations the order with which each of the above design criteria was applied was altered. Each time this 20 was done the primary goal however was to increase the ability of the Savine to cater for interclade differences. Two isolate sequences, GenBank accession U51189 and U46016, for clade E and clade C, respectively, were used when a consensus sequence for some HIV proteins from these two clades was unavailable (Gao et al., 1996; Salminen et al., 1996). The design of a consensus sequence for the hypervariable regions of the HIV envelope protein and in some cases between these regions (hypervariable regions 1-2 and 3-5) was difficult and so these regions were excluded from the vaccine design.

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Once a degenerate consensus sequence was designed for each HIV protein, an approach was then determined for incorporating all the protein sequences safely into the vaccine. One convenient approach to ensure that a vaccine will be safe is to systematically fragment and randomly rearrange the protein sequences together thus abrogating or otherwise altering their structure and function. The protein sequences still have to be immunologically functional however, meaning that the process used to fragment the

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sequences should not destroy potential epitopes. To decide on the best approach for systematically fragmenting protein sequences, the main criteria used was the size of T epitopes and their processing requirements. Class I-restricted T cell epitopes are 8-10 amino acids long and generally require 2-3 natural flanking amino acids to ensure their efficient processing and presentation if placed next to unnatural flanking residues (Del Val et al., 1991; Thomson et al., 1995). Class II-restricted T cell epitopes range between 12-25 amino acids long and do appear to require natural flanking residues for processing however, it is difficult to rule out a role for natural flanking residues in all cases due to the complexity of their processing pathways (Thomson et al., 1998). Also class II-restricted epitopes despite being larger than CTL epitopes generally have a core sequence of 9-10 amino acids, which binds to MHC molecules in a sequence specific fashion. Thus, based on current knowledge, it was decided that an advantageous approach was to overlap the fragments by at least 15 amino acids to ensure that potential epitopes which might lie across fragment boundaries are not lost and to ensure that CTL epitopes near fragment boundaries, that are placed beside or near inhibitory amino acids in adjacent fragments, are processed efficiently. In deciding the optimal fragment size, the main criteria used were that size had to be small enough to cause the maximum disruption to the structure and function of proteins but large enough to cover the sequence information as efficiently as possible without any further unnecessary duplication. Based on these criteria the fragments would be twice the overlap size, in this case 30 amino acids long.

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The designed degenerate protein sequences were then separated into fragments 30 amino acid long and overlapping by fifteen amino acids. Two alanine amino acids were also added to the start and end of the first and last fragment for each protein or envelop protein segment to ensure these fragments were not placed directly adjacent to amino acids capable of blocking epitope processing (Del Val et al., 1991). The next step was to reverse translate each protein sequence back into DNA. Duplicating DNA sequences was avoided when constructing DNA sequences encoding a tandem repeat of identical or homologous amino acid sequences to maximise expression of the Savine. In this regard, the first and second most commonly used mammalian codons (shown in Figure 12) were assigned to amino acids in these repeat regions, wherein a first codon was used to encode an amino acid in one of the repeated sequences and wherein a second but synonymous codon was used for the other repeated sequence (e.g., see the gag HIV protein in Figure 13). To cater

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for the designed amino acid mutations more than one base was assigned to some positions using the IUPAC DNA codes without exceeding more than three base variations (eight possible combinations) in any group of 27 bases (Figure 12). Where a particular combination of amino acids could not be incorporated, because too many degenerate bases would be required, some or all of the amino acid degeneracy was removed according to the protein consensus design rules outlined above. Also the degenerate codons were checked to determine if they could encode a stop codon, if stop codons could not be avoided then the amino acid degeneracy was also simplified again according to the protein consensus design rules outlined above.

The designed DNA segments were then scrambled randomly and joined to create twenty-two subcassettes approximately 840 bp in size. Extra DNA sequences incorporating sites for one of the cohesive restriction enzymes XbaI, SpeI, AvrII or NheI and 3 additional base pairs (to cater for premature Taq polymerase termination) were then added to each end of each subcassette (Figure 14). Some of these extra DNA sequences also contained, the cohesive restriction sites for SaII or XhoI, Kozak signal sequences and start or stop codons to enable the subcassettes to be joined and expressed either as three large cassettes or one full length protein (Figures 14 and 15).

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In designing the HIV Savine one issue that required investigation was whether such a large DNA molecule would be fully expressed and whether epitopes encoded near the end of the molecule would be efficiently presented to the immune system. The inventors also wished to show that mixing two or more degenerate Savine constructs together could induce T cell responses that recognise mutated sequences. To examine both issues DNA coding for a degenerate murine influenza nucleoprotein CTL epitope, NP365-373, which differs by two amino acids at positions 71 and 72 in influenza strain A/PR/8/34 compared to the A/NT/60/68strain and restricted by H2-Db, was inserted before the last stop codon at the end of the HIV Savine design (Figure 15). An important and unusual characteristic of both of these naturally occurring NP365-373 sequences, which enabled the present inventors to examine the effectiveness of incorporating mutated sequences, is that they generate CTL responses which do not cross react with the alternate sequence (Townsend et. al., 1986). This is an unusual characteristic because epitopes not destroyed by mutation usually induce CTL responses that cross-react.

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Up to ten long oligonucleotides up to 100 bases long and two short amplification oligonucleotides were synthesised to enable construction of each subcassette (Life Technologies). In designing each oligonucleotide the 3' end and in most cases also the 5' end had to be either a 'c' or a 'g' to ensure efficient extension during PCR splicing. The overlap region for each long oligonucleotide was designed to be at least 16 bp with approximately 50% G/C content. Also oligonucleotide overlaps were not placed where degenerate DNA bases coded for degenerate amino acids to avoid splicing difficulties later. Where this was too difficult some degenerate bases were removed according to the protein consensus design rules outlined above and indicated in Figure 12. Figure 16 shows an example of the oligonucleotides design for each subcassette.

## Construction of the HIV Savine

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Five of each group of ten designed oligonucleotides were spliced together using stepwise asymmetric PCR (Sandhu et al., 1992) and Splicing by Overlap Extension (SOEing) (Figure 17a). Each subcassette was then PCR amplified, cloned into pBluescript™ II KS- using BamHI/EcoRI and 16 individual clones sequenced. Mutations, deletions and insertions were present in the large majority of the clones for each subcassette, despite acrylamide gel purification of the long oligonucleotides. In order to construct a functional Savine with minimal mutations, two clones for each subcassette with no insertions or deletions and hence a complete open reading frame and with minimal numbers of non-designed mutations, were selected from the sixteen available. The subcassettes were then excised from their plasmids and joined by stepwise PCR-amplified ligation using the polymerase blend Elongase™ (Life Technology), T4 DNA ligase and the cohesive restriction enzymes Xbal/Spel/AvrII/NheI, to generate two copies of cassettes A, B and C as outlined in Figure 14 and shown in Figure 17b. Predicted sequences for these cassettes are shown in Figure 30. Each cassette was then reamplified by PCR with Elongase™, cloned into pBluescript™ II KS- and 3 of the resulting plasmid clones sequenced using 12 of the 36 sequencing primers designed to cover the full length construct. Clones with minimal or no further mutations were selected for transfer into plasmids for DNA vaccination or used to make recombinant poxviruses. A summary of the number of designed and non-designed mutations in each Savine construct is presented in Table 1.

TABLE 1
Summary of mutations

Construct	No. 125	Names of municus			
		Designed	Expected in 2 clones	Actual in 2 closes	Non-designed
Cassette A	1896	249	124	107	5 (AC1), 8 (AC2)
Cassette B	1184	260	130	124	11 (BC1), 4 (BC2)
Cassette C	1969	276	138	121	10 (CC1), 14 (CC2)
Full length	5742	785	392	352	26 (FL1), 26 (FL2)

Summary of the mutations present in the two full-length clones constructed as determined by sequencing. Includes the number of mutations designed, expected and actually present in the 2 clones and the number of non-designed mutations in each cassette and full-length clone.

#### HIV Savine DNA vaccines and Recombinant Vaccinia viruses

To test the immunological effectiveness of the HIV Savine constructs the cassette sequences were transferred into DNA vaccine and poxvirus vectors. These vectors when used either separately in immunological assays described below or together in a 'prime-boost' protocol which has been shown previously to generate strong T cell responses in vivo (Kent et al., 1997).

DNA Vaccination plasmids were constructed by excising the cassettes from the selected plasmid clones with XbaI/XhoI (cassette A) or XbaI/SaII (cassettes B and C) and ligating them into pDNAVacc cut with XbaI/XhoI to create pDVAC1, pDVAC2, pDVBC1, pDVBC2, pDVCC1, pDVCC2, respectively (Figure 18a). These plasmids were then further modified by cloning into their XbaI site a DNA fragment excised using XbaI/AvrII from pTUMERA2 and encoding a synthetic endoplasmic reticulum (ER) signal sequence from the Adenovirus E1A protein (Persson et al., 1980) (Figure 18a). ER signal sequences have been shown previously to enhance the presentation of both CTL and T helper epitopes in vivo (Ishioka, G.Y., 1999; Thomson et al., 1998). The plasmids pDVERAC1, pDVERBC1, pDVERCC1 andpDVERAC2, pDVERBC2, pDVERCC2 were then mixed

together to create, plasmid pool 1 and pool 2 respectively. Each plasmid pool collectively encodes one copy of the designed full-length HIV Savine.

Plasmids to generate recombinant Vaccinia viruses which express HIV Savine sequences were constructed by excising the various HIV Savine cassettes from the selected plasmid clones using BamHI/XhoI (cassette A) or BamHI/SaII (cassettes B and C) and cloned into the marker rescue plasmid, pTK7.5, cleaved with BamHI/SalI. These pTK7.5derived plasmids were then used to generate recombinant Vaccinia viruses by marker rescue recombination using established protocols (Boyle et al., 1985) to generate VV-AC1, VV-AC2, VV-BC1, VV-BC2, VV-CC1 and VV-CC2 (Figure 18b).

Two further DNA vaccine plasmids were constructed each encoding a version of the full length HIV Savine (Figure 18c). Briefly, the two versions of cassette B were excised with XhoI and cloned into the corresponding selected plasmid clones containing cassette A sequences that were cut with XhoUSaII to generate pBSAB1 and pBSAB2 respectively. The joined A/B cassettes in pBSAB1 and pBSAB2 were excised with 15 Xbal/XhoI and cloned into pDVCC1 and pDVCC2, respectively, and cleaved with Xbal/XhoI to generate pDVFL1 and pDVFL2. These were then further modified to contain an ER signal sequence using the same cloning strategy as outlined in figure 18a.

### Restimulation of HIV specific lymphocytes from HIV infected patients

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The present inventors examined the capacity of the HIV Savine to restimulate 20 HIV-specific polyclonal CTL responses from HIV-infected patients. PBMCs from three different patients were restimulated in vitro with two HIV Savine Vaccinia virus pools (Pool 1 included VV-AC1 and VV-BC1; Pool 2 included VV-AC2, VV-BC2 and VV-CC2) then used in CTL lysis assays against LCLs infected either with one of the Savine Vaccinia virus pools or Vaccinia viruses which express gag, env or pol. Figure 19 clearly shows, 25 that in all three assays, both HIV Savine viral pools restimulated HIV-specific CTL responses which could recognise targets expressing whole natural HIV antigens and not targets which were uninfected or infected with the control Vaccinia virus. Furthermore, in all three cases, both pools restimulated responses that recognised all three natural HIV antigens. This result suggests that the combined Savine constructs will provide broader 30 immunological coverage than single antigen based vaccine approaches. The level of lysis in each case of targets infected with Savine viral pools was significantly higher than the

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lysis recorded for any other infected target. This probably reflects the combined CTL responses to gag, pol, and env plus other HIV antigens not analysed here but whose sequences are also incorporated into the Savine constructs.

CTL recognition of each HIV antigen is largely controlled by each patient's HLA 5 background hence the pattern of CTL lysis for whole HIV antigens is different in each patient. Interestingly, this CTL lysis pattern did not change when the second Savine Vaccinia virus pool was used for CTL restimulation. In these assays, therefore, the inventors were unable to demonstrate clear differences between pools 1 and 2, despite pool 1 lacking a Vaccinia virus expressing cassette CC1 and despite the many amino acid differences between the A and B cassettes in each pool (see table 1).

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From the foregoing, the present inventors have developed a novel vaccine/therapeutic strategy. In one embodiment, pathogen or cancer protein sequences are systemically fragmented, reverse translated back into DNA, rearranged randomly then joined back together. The designed synthetic DNA sequence is then constructed using long oligonucleotides and can be transferred into a range of delivery vectors. The vaccine vectors used here were DNA vaccine plasmids and recombinant poxvirus vectors which have been previously shown to elicit strong T cell responses when used together in a 'prime-boost' protocol (Kent et al., 1997). An important advantage of scrambled antigen vaccines or 'Savines' is that the amount of starting sequence information for the design can be easily expanded to include the majority of the protein sequences from a pathogen or for cancer, thereby providing the maximum possible vaccine or therapy coverage for a given population.

An embodiment of the systematic fragmentation approach described herein was based on the size and processing requirements for T cell epitopes and was designed to 25 cause maximal disruption to the structure and function of protein sequences. This fragmentation approach ensures that the maximum possible range of T cell epitopes will be present from any incorporated protein sequence without the protein being functional and able to compromise vaccine safety

Another important advantage of Savines is that consensus protein sequences can be used for their design. This feature is only applicable when the design needs to cater for pathogen or cancer antigens whose sequence varies considerably. HIV is a highly

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mutagenic virus, hence this feature was utilised extensively to design a vaccine which has the potential to cover not only field isolates of HIV but also the major HIV clades involved in the current HIV pandemic. To construct the HIV Savine, one set of long oligonucleotides was synthesised, which included degenerate bases in such a way that 8 constructs are theoretically required for the vaccine to contain all combinations in any stretch of 9 amino acids. The inventors believe that this approach can be improved for the following reasons: 1) While degenerate bases should be theoretically equally represented, in practice some degenerate bases were biased towards one base or the other, leading to a lower than expected frequency of the designed mutations in the two full length HIV Savines which were constructed (see Table 1). 2) Only sequence combinations actually present in the HIV clade consensus sequences are required to get full clade coverage, hence the number of full length constructs needed could be reduced. To reduce the number of constructs however, separate sets of long oligonucleotides would have to be synthesised, significantly increasing the cost, time and effort required to generate a vaccine capable of such considerable vaccine coverage.

A significant problem during the construction of the HIV Savine synthetic DNA sequence was the incorporation of non-designed mutations. The most serious types of mutations were insertions, deletions or those giving rise to stop codons, all of which change the frame of the synthesised sequences and/or caused premature truncation of the Savine proteins. These types of mutation were removed during construction of the HIV Savines by sequencing multiple clones after subcassette and cassette construction and selecting functional clones. The major source of these non-designed mutations was in the long oligonucleotides used for Savine synthesis, despite their gel purification. This problem could be reduced by making the initial subcassettes smaller thereby reducing the possibility of corrupted oligonucleotides being incorporated into each subcassette clone. The second major cause of non-designed mutations was the large number of PCR cycles required for the PCR and ligation-mediated joining of the subcassettes. Including extra sequencing and clone selection steps during the subcassette joining process should help to reduce the frequency of non-designed mutations in future constructs. Finally, another method that could help reduce the frequency of such mutations at all stages is to use resolvase treatment. Resolvases are bacteriophage-encoded endonucleases which recognise disruptions to double stranded DNA and are primarily used by bacteriophages to resolve

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Holliday junctions (Mizuuchi, 1982; Youil et al., 1995). T7 endonuclease I has already been used by the present inventors in synthetic DNA constructions to recognise mutations and cleave corrupted dsDNA to allow gel purification of correct sequences. Cleavage of corrupted sequences occurs because after a simple denaturing and hybridisation step mutated DNA hybridises to correct DNA sequences and results in a mispairing of DNA bases which is able to be recognised by the resolvase. This method resulted in a 50% reduction in the frequency of errors. Further optimisation of this method and the use of a thermostable version of this type of enzyme could further reduce the frequency of errors during long Savine construction.

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Two pools of Vaccinia viruses expressing Savine cassettes were both shown to restimulate HIV-specific responses from three different patients infected with B clade HIV viruses. These results provide a clear indication that the HIV Savine should provide broad coverage of the population because each patient had a different HLA pattern yet both pools were able to restimulate HIV-specific CTL responses in all three patients against all three natural HIV proteins tested. Also, both pools were shown to restimulate virtually identical CTL patterns in all three patients. This result was unexpected because some responses should have been lost or gained due to the amino acid differences between the two pools and because Pool 1 is only capable of expressing 2/3 of the full length HIV Savine. There are two suggested reasons why the pattern of CTL lysis was not altered between the two viral pools. Firstly, the sequences in the Savine constructs are nearly all duplicated because the fragment sequences overlap. Hence the loss of a third of the Savine may not have excluded sufficient T cell epitopes for differences to be detected in only three patient samples against only three HIV proteins. Secondly, while mutations often destroy T cell epitopes, if they remain functional, then the CTL they generate frequently can recognise alternate epitope sequences. Taken together this finding indirectly suggests that combining only two Savine constructs may provide robust multiclade coverage. Further experiments are being carried out to directly examine the capacity of the HIV Savine to stimulate CTL generated by different strains of HIV virus. The capacity of the two HIV-1 Savine Vaccinia vector pools to stimulate CD4+ T cell HIV-1 specific responses from infected patients was also tested (Figure 20). Both patients showed significant proliferation of CD4+ T cells although both pools did not show consistent patterns suggesting that the two pools may provide wider vaccine coverage than using either pool independently.

The present inventors have generated a novel vaccine strategy, which has been used to generate what the inventors believe to be the most effective HIV candidate vaccine to date. The inventors have used this vaccine to immunise naive mice. Figure 21 shows conclusively that the HIV-1 Savine described above can generate a Gag and Nef CTL response in naïve mice. It should be noted, however, that the Nef CTL epitope appeared to exist only in Pool 1 since it was not restimulated by Pool 2. This is further proof of the utility of combining HIV-1 Savine Pool 1 and Pool 2 components together to provide broader vaccine coverage.

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The HIV-1 Savine Vaccinia vectors have also been used to restimulate *in vivo*10 HIV-1 responses in pre-immune *M. nemestrina* monkeys. These experiments (Figure 22) showed, by INF-γ ELISPOT and CD69 expression on both CD4 and CD8 T cells, that the ability of the HIV-1 SAVINE to restimulate HIV-1 specific responses in vivo is equivalent or perhaps better than another HIV-1 candidate vaccine.

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This is a generic strategy able to be applied to many other human infections or cancers where T-cell responses are considered to be important for protection or recovery. With this in mind the inventors have begun constructing Savines for melanoma, cervical cancer and Hepatitis C. In the case of melanoma, the majority of the currently identified melanoma antigens have been divided into two groups, one containing antigens associated with melanoma and one containing differentiation antigens from melanocytes, which are often upregulated in melanomas. Two Savine constructs are presently being constructed to cater for these two groups. The reason for making the distinction is that treatment of melanoma might first proceed using the Savine that incorporates fragments of melanoma specific antigens only. If this Savine fails to control some metastases then the less specific Savine containing the melanocyte-specific antigens can then be used. It is important to point out that other cancers also express many of the antigens specific to melanomas e.g., testicular and breast cancers. Hence the melanoma specific Savine may have therapeutic benefits for other cancers.

A small Savine is also being constructed for cervical cancer. This Savine will contain two antigens, E6 and E7, from two strains of human papilloma virus (HPV), HPV-16 and HPV-18, directly linked with causing the majority of cervical cancers worldwide. There is a large number of sequence differences in these two antigens between the two

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strains which would normally require two Savines to be constructed. However since this Savine is small, the antigen fragments from both strains are being scrambled together. While it is normally better for the Savine approach to include all or a majority of the antigens from a virus, in this case only E6 and E7 are expressed during viral latency or in cervical carcinomas. Hence in the interests of simplicity, the rest of the HPV genome will not be included although all HPV antigens would be desirable in a Savine against genital warts.

Two Savines have also been constructed for two strains of hepatitis C, a major cause of liver disease in the world. Hepatitis C is similar to HIV in the requirements for a vaccine or therapeutic. However, the major hepatitis C strains share significantly lower homology, 69-79%, with one another than do the various HIV clades. To cater for this the inventors have decided to construct two separate constructs to cater for the two major strains present in Australia, types 1 aand 3a, which together cause approximately 80-95% of hepatitis C infections in this country. Both constructs will be approximately the same size as the HIV Savine but will be blended together into a single vaccine or therapy.

Overall it is believed that the Savine vaccine strategy is a generic technology likely to be applied to a wide range of human diseases. It is also believed that because it is not necessary to characterise each antigen, this technology will be actively applied to animal vaccines as well where research into vaccines or therapies is often inhibited by the lack of specific reagents, modest research budgets and poor returns on animal vaccines.

#### **EXAMPLE 2**

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### Hepatitis C Savine

Synthetic immunomodulatory molecules have also been designed for treating Hepatitis C. In one example, the algorithm of Figure 25 was applied to a consensus polyprotein sequence of Hepatitis C 1a to facilitate its segmentation into overlapping segments (30 aa segments overlapping by 15 aa), the rearrangement of these segments into a scrambled order and the output of Savine nucleic acid and amino acid sequences, as shown in Figure 26. Exemplary DNA cassettes (A, B and C) are also shown in Figure 26, which contain suitable restriction enzyme sites at their ends to facilitate their joining into a single expressible open reading frame.

## EXAMPLE 3

### Melanoma Savine

The algorithm of Figure 25 was also applied to melanocyte differentiation antigens (gp100, MART, TRP-1, Tyros, Trp-2, MC1R, MUC1F and MUC1R) and to melanoma specific antigens (BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b and LAGE1), as shown in Figure 27, to provide separate Savine nucleic acid and amino acid sequences for treating or preventing melanoma.

#### **EXAMPLE 4**

### Resolvase Repair Experiment

10 A resolvase can be used advantageously to repair errors in polynucleotides. The following procedure outlines resolvase repair of a synthetic 340 bp fragment in which DNA errors were common.

### Method

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The 340 bp fragment was PCR amplified and gel purified on a 4% agarose gel. 15 After spin purifying, 10ul of the eluate corresponding to approximately 100 ng was subjected to the resolvase repair treatment. The rest of the DNA sample was stored for later cloning as the untreated control.

2 μL of 10xPCR buffer, 2 μL of 20 mM MgCl<sub>2</sub> and 6 μL of MilliQ<sup>TM</sup> water (MQW) and Taq DNA polymerase were added to the 10 µL DNA sample. The mixture was subjected to the following thermal profile; 95°C for 5min, 65°C for 30min, cooled and held at 37°C. Five μL of 10xT7 endonuclease I buffer, 8 μL of 1/50 μL of T7endoI enzyme stock and 17 µL of MQW were added, mixed and incubated for 30 min. Loading buffer was added to the sample and the sample was electrophoresed on a 4% agarose gel. A faint band corresponding to the full length fragment was excised and subjected to 15 further 25 cycles of PCR. The amplified fragment was agarose gel purified and, along with the untreated DNA sample, cloned into pBluescript. Eleven plasmid clones for each DNA sample were sequenced and the number and type of errors compared (see table)

Buffers were as follows:

# 10x T7endonuclease buffer

2.5ml 1M TRIS pH7.8, 0.5ml 1M MgCl<sub>2</sub>, 25  $\mu$ L 1 M DTT, 50  $\mu$ L 10mg/mL BSA, 2 mL MQW made up to a total of 5 mL.

## 5 T7 endonuclease I stock

Concentrated sample of enzyme prepared by, and obtained from, Jeff Babon (St Vincent's Hospital) was diluted 1/50 using the following dilution buffer: 50  $\mu$ L 1 M TRIS pH7.8, 0.1 $\mu$ L 1M EDTA pH8, 5  $\mu$ L 100 mM glutathione, 50  $\mu$ L 10mg/mL BSA, 2.3 mL MQW, 2.5 mL glycerol made up to a total of 5 mL.

## 10 Results

The results are summarised in Tables 2 and 3.

TABLE 2

Tod Ecros				
Universed	Resolvance mented			
A/T to $G/C = 6$	A/T to G/C = 1			
G/C to A/T = 12	G/C to $A/T = 7$			
A/T to deletion = 1	A/T to deletion = 1			
G/C to deletion = 6	G/C to deletion = 3			

TABLE 3

Tole summery				
Urrensi	Resolvence restred			
6/11 contained deletions	3/11 contained deletions			
9/11 contained mutations	7/11 contained mutations			

Cloue sommery				
Untreased	Resolvane treated			
2/11 correct	3/11 correct			

### Discussion/Conclusion

While overall the number of correct clones obtained was not significantly different, there was a significant difference in the level of errors. This reduction in errors becomes more significant as greater numbers of long oligonucleotides are joined into the one construct *i.e.*, increasing the difference between untreated *versus* treated samples in the chance of obtaining a correct clone. It is believed that combining another resolvase such as T4 endonuclease VII may further enhance repair or increase the bias against errors.

Importantly, this experiment was not optimised e.g., by using proofreading PCR enzymes or optimised conditions. Finally if the repair reaction is carried out during normal PCR, for example, by including a thermostable resolvase, it is believed that amplification of already damaged long oligonucleotides, and the normal accumulation of PCR induced errors, even using error reading polymerases during PCR, could be reduced significantly. The repair of damaged long oligonucleotides is particularly important for synthesis of long DNA fragment such as in Savines because, while the rate of long oligonucleotide damage is typically <5%, after joining 10 oligonucleotides, the error rate approaches 50%. This is true even using the best proofreading PCR enzymes because these enzymes do not verify the sequence integrity using correct oligonucleotide templates that exist as a significant majority (95%) in a joining reaction.

The disclosure of every patent, patent application, and publication cited herein is incorporated herein by reference in its entirety.

The citation of any reference herein should not be construed as an admission that such reference is available as "Prior Art" to the instant application

Throughout the specification the aim has been to describe the preferred embodiments of the invention without limiting the invention to any one embodiment or specific collection of features. Those of skill in the art will therefore appreciate that, in

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light of the instant disclosure, various modifications and changes can be made in the particular embodiments exemplified without departing from the scope of the present invention. All such modifications and changes are intended to be included within the scope of the appended claims.

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#### WHAT IS CLAIMED IS:

- 1. A synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide.
- 2. The synthetic polypeptide of claim 1, consisting essentially of different segments of a single parent polypeptide.
- 3. The synthetic polypeptide of claim 1, consisting essentially of different segments of a plurality of different parent polypeptides.
- 4. The synthetic polypeptide of claim 1, wherein the segments in said synthetic polypeptide are linked sequentially in a different order or arrangement relative to their linkage in said at least one parent polypeptide.
- 5. The synthetic polypeptide of claim 4, wherein the segments in said synthetic polypeptide are randomly rearranged relative to their order or arrangement in said at least one parent polypeptide.
- 6. The synthetic polypeptide of claim 1, wherein the size of an individual segment is at least 4 amino acids.
- 7. The synthetic polypeptide of claim 6, wherein the size of an individual segment is from about 20 to about 60 amino acids.
- 8. The synthetic polypeptide of claim 7, wherein the size of an individual segment is about 30 amino acids.
- 9. The synthetic polypeptide of claim 7, comprising at least 30% of the parent polypeptide sequence.
- 10. The synthetic polypeptide of claim 1, wherein at least one of said segments comprises partial sequence identity or homology to one or more other said segments.
- 11. The synthetic polypeptide of claim 10, wherein the sequence identity or homology is contained at one or both ends of an individual segment.

- 12. The synthetic polypeptide of claim 11, wherein one or both ends of said segment comprises at least 4 contiguous amino acids that are identical to, or homologous with, an amino acid sequence contained within one or more other of said segments.
- 13. The synthetic polypeptide of claim 10, wherein the size of an individual segment is about twice the size of the sequence that is identical or homologous to the or each other said segment.
- 14. The synthetic polypeptide of claim 13, wherein the size of an individual segment is about 30 amino acids and the size of the sequence that is identical or homologous to the or each other said segment is about 15 amino acids.
- 15. The synthetic polypeptide of claim 1, wherein an optional spacer is interposed between some or all of the segments.
- 16. The synthetic polypeptide of claim 15, wherein the spacer alters proteolytic processing and/or presentation of adjacent segment(s).
- 17. The synthetic polypeptide of claim 16, wherein the spacer comprises at least one neutral amino acid.
- 18. The synthetic polypeptide of claim 16, wherein the spacer comprises at least one alanine residue.
- 19. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is associated with a disease or condition.
- 20. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is selected from a polypeptide of a pathogenic organism, a cancer-associated polypeptide, an autoimmune disease-associated polypeptide, an allergy-associated polypeptide or a variant or derivative of these.
- 21. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is a polypeptide of a virus.
- 22. The synthetic polypeptide of claim 21, wherein the virus is selected from a Human Immunodeficiency Virus (HIV) or a Hepatitis virus.
- 23. The synthetic polypeptide of claim 22, wherein the virus is a Human Immunodeficiency Virus (HIV) and the at least one parent polypeptide is selected from env, gag, pol, vif, vpr, tat, rev, vpu and nef, or a combination thereof.

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- 24. The synthetic polypeptide of claim 1, wherein the at least one parent polypeptide is a cancer-associated polypeptide.
- 25. The synthetic polypeptide of claim 24, wherein the cancer is melanoma.
- 26. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanocyte differentiation antigen.
- 27. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanocyte differentiation antigen selected from gp100, MART, TRP-1, Tyros, TRP2, MC1R, MUC1F, MUC1R or a combination thereof.
- 28. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanoma-specific antigen.
- 29. The synthetic polypeptide of claim 25, wherein the at least one parent polypeptide is a melanoma-specific antigen selected from BAGE, GAGE-1, gp100In4, MAGE-1, MAGE-3, PRAME, TRP2IN2, NYNSO1a, NYNSO1b, LAGE1 or a combination thereof.
- 30. A synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide.
- 31. A method for producing the synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, said method comprising:
  - linking together in the same reading frame a plurality of nucleic acid sequences encoding different segments of the at least one parent polypeptide to form a synthetic polynucleotide whose sequence encodes said segments linked together in a different relationship relative to their linkage in the at least one parent polypeptide.
- 32. The method of claim 31, further comprising fragmenting the sequence of a respective parent polypeptide into fragments and linking said fragments together in a different relationship relative to their linkage in a respective parent polypeptide sequence.

- 33. The method of claim 32, wherein the fragments are randomly linked together.
- 34. The method of claim 31, further comprising reverse translating the sequence of a respective parent polypeptide or a segment thereof to provide a nucleic acid sequence encoding said parent polypeptide or said segment.
- 35. The method of claim 34, wherein an amino acid of a respective parent polypeptide sequence is reverse translated to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest.
- 36. The method of claim 35, wherein an amino acid of said parent polypeptide sequence is reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence that is refractory to the execution of a task.
- 37. The method of claim 35, wherein an amino acid of said parent polypeptide sequence is reverse translated to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence selected from a palindromic sequence or a duplicated sequence, which is refractory to the execution of a task selected from cloning or sequencing.
- 38. The method of claim 31, further comprising linking a spacer oligonucleotide encoding at least one spacer residue between segment-encoding nucleic acids.
- 39. The method of claim 38, wherein spacer oligonucleotide encodes 2 to 3 spacer residues.
- 40. The method of claim 38 or claim 39, wherein the spacer residue is a neutral amino acid.
- 41. The method of claim 38 or claim 39, wherein the spacer residue is alanine.
- 42. The method of claim 31, further comprising linking in the same reading frame as other segment-containing nucleic acid sequences at least one variant nucleic acid sequence which encodes a variant segment having a homologous but not identical amino acid sequence relative to other encoded segments.

- 43. The method of claim 42, wherein the variant segment comprises conserved and/or non-conserved amino acid differences relative to one or more other encoded segments.
- 44. The method of claim 43, wherein the differences correspond to sequence polymorphisms.
- 45. The method of claim 44, wherein degenerate bases are designed or built in to the at least one variant nucleic acid sequence to give rise to all desired homologous sequences.
- 46. The method of claim 31, further comprising optimising the codon composition of the synthetic polynucleotide such that it is translated efficiently by a host cell.
- 47. A synthetic construct comprising a synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, wherein said synthetic polynucleotide is operably linked to a regulatory polynucleotide.
- 48. The synthetic construct of claim 47, further including a nucleic acid sequence encoding an immunostimulatory molecule.
- 49. The synthetic construct of claim 48, wherein the immunostimulatory molecule comprises a domain of an invasin protein (Inv).
- 50. The synthetic construct of claim 48, wherein the immunostimulatory molecule comprises the sequence set forth in SEQ ID NO: 1467 or an immune stimulatory homologue thereof.
- 51. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a T cell co-stimulatory molecule.
- 52. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a T cell co-stimulatory molecule selected from a B7 molecule or an ICAM molecule.
- 53. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a B7 molecule or a biologically active fragment thereof, or a variant or derivative of these.

- 54. The synthetic construct of claim 48, wherein the immunostimulatory molecule is a cytokine selected from an interleukin, a lymphokine, tumour necrosis factor or an interferon.
- 55. The synthetic construct of claim 48, wherein the immunostimulatory molecule is an immunomodulatory oligonucleotide.
- 56. An immunopotentiating composition, comprising an immunopotentiating agent selected from the synthetic polypeptide of claim 1, the synthetic polynucleotide of claim 30 or the synthetic construct of claim 47, together with a pharmaceutically acceptable carrier.
- 57. The composition of claim 56, further comprising an adjuvant.
- 58. A method for modulating an immune response, which response is preferably directed against a pathogen or a cancer, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from the synthetic polypeptide of claim 1, the synthetic polynucleotide of claim 30, the synthetic construct of claim 47, or the composition of claim 56.
- 59. A method for treatment and/or prophylaxis of a disease or condition, comprising administering to a patient in need of such treatment an effective amount of an immunopotentiating agent selected from selected from the synthetic polypeptide of claim 1, the synthetic polynucleotide of claim 30, the synthetic construct of claim 47, or the composition of claim 56.
- 60. A computer program product for designing the sequence of a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, said program product comprising:
  - code that receives as input the sequence of said at least one parent polypeptide;
  - code that fragments the sequence of a respective parent polypeptide into fragments;
  - code that links together said fragments in a different relationship relative to their linkage in said parent polypeptide sequence; and

- a computer readable medium that stores the codes.
- 61. The computer program product of claim 60, further comprising code that randomly rearranges said fragments.
- 62. The computer program product of claim 60, further comprising code that links the sequence of a spacer residue to the sequence of said at least one parent polypeptide or to said fragments.
- 63. A computer program product for designing the sequence of a synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, comprising:
  - code that receives as input the sequence of at least one parent polypeptide;
  - code that fragments the sequence of a respective parent polypeptide into fragments;
  - code that reverse translates the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment;
  - code that links together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence; and
    - a computer readable medium that stores the codes.
- 64. The computer program product of claim 63, further comprising code that randomly rearranges said nucleic acid sequences.
- 65. The computer program product of claim 64, further comprising code that reverse translates an amino acid of a respective parent polypeptide sequence to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest.
- 66. The computer program product of claim 63, further comprising code that reverse translates an amino acid of a respective parent polypeptide sequence to provide a codon

which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence that is refractory to the execution of a task.

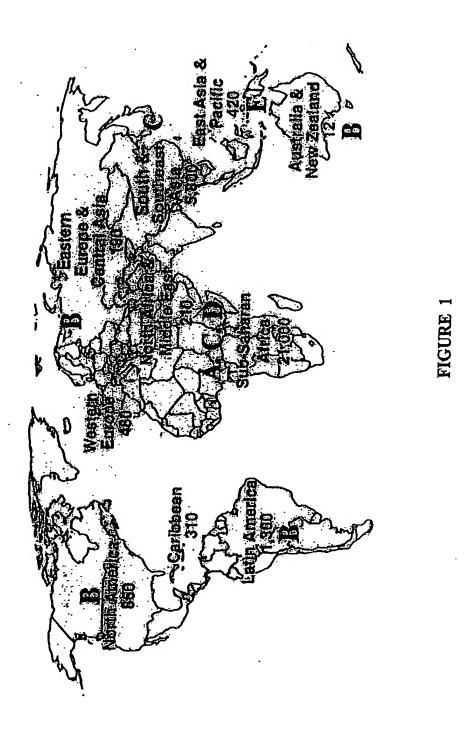
- 67. The computer program product of claim 63, further comprising code that links a spacer oligonucleotide to one or more of said nucleic acid sequences.
- 68. A computer for designing the sequence of a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, wherein said computer comprises:
  - (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
  - (b) a working memory for storing instructions for processing said machine-readable data;
  - (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polypeptide sequence; and
  - (d) an output hardware coupled to said central processing unit, for receiving said synthetic polypeptide sequence.
- 69. The computer of claim 68, wherein the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments and linking together said fragments in a different relationship relative to their linkage in the sequence of said parent polypeptide.
- 70. The computer of claim 68, wherein the processing of said machine readable data comprises randomly rearranging said fragments.
- 71. The computer of claim 68, wherein the processing of said machine readable data comprises linking the sequence of a spacer residue to the sequence of said at least one parent polypeptide or to said fragments.

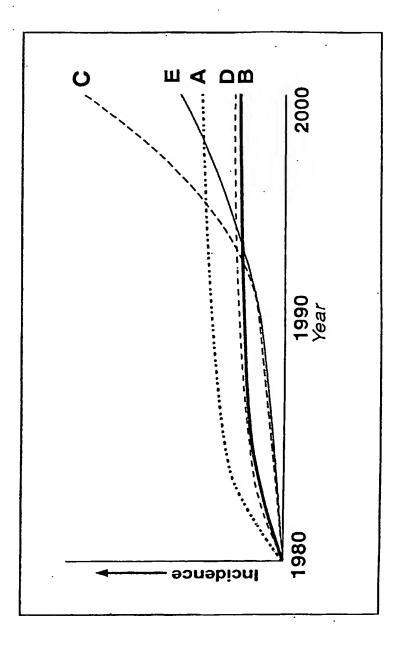
- 72. A computer for designing the sequence of a synthetic polynucleotide encoding a synthetic polypeptide comprising a plurality of different segments of at least one parent polypeptide, wherein the segments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide to impede, abrogate or otherwise alter at least one function associated with the parent polypeptide, wherein said computer comprises:
  - (a) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise the sequence of at least one parent polypeptide;
  - (b) a working memory for storing instructions for processing said machine-readable data;
  - (c) a central-processing unit coupled to said working memory and to said machinereadable data storage medium, for processing said machine readable data to provide said synthetic polynucleotide sequence; and
  - (d) an output hardware coupled to said central processing unit, for receiving said synthetic polynucleotide sequence.
- 73. The computer of claim 72, wherein the processing of said machine readable data comprises fragmenting the sequence of a respective parent polypeptide into fragments, reverse translating the sequence of a respective fragment to provide a nucleic acid sequence encoding said fragment and linking together in the same reading frame each said nucleic acid sequence to provide a polynucleotide sequence that codes for a polypeptide sequence in which said fragments are linked together in a different relationship relative to their linkage in the at least one parent polypeptide sequence.
- 74. The computer of claim 72, wherein the processing of said machine readable data comprises randomly rearranging said nucleic acid sequences.
- 75. The computer of claim 72, wherein the processing of said machine readable data comprises reverse translating an amino acid of a respective parent polypeptide sequence to provide a codon, which has higher translational efficiency than other synonymous codons in a cell of interest.

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76. The computer of claim 72, wherein the processing of said machine readable data comprises reverse translating an amino acid of a respective parent polypeptide sequence to provide a codon which, in the context of adjacent or local sequence elements, has a lower propensity of forming an undesirable sequence that is refractory to the execution of a task.

77. The computer of claim 72, wherein the processing of said machine readable data comprises linking a spacer oligonucleotide to one or more of said nucleic acid sequences.





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14-
                          nls
               membrane binding
 DESIGNED SEQ MGARASVLSGGKLDAMEKIRLRPGGKKKYMOKHLVWASRELERPALNPGLLETAEGCQQILEQLQSALKT
                              RL I S S K G P Q
 MUTATED AAS
          MGARASVI.SGKI.DANEKI RI.RPGGKKKYKMKHILVWASRELERFALNPGILETAEGCQQLIEQI.QSTLKT
                                                               70
 E-ISOLATE
         mGARaSvLsggklDawekIrlRPgGkKkYrlKHlvwAsreLerPaLnPslLeTaegcgqimeQlqsalkT
                                                               70
 CONSENSUS-A
          -----i-r---?------h-Mi-------g---s--k--ik---P--0
 CONSENSUS-B
                                                               70
 CONSENSUS-C
                                                               69
         68
 CONSENSUS-D
                                                               70
 CONSENSUS-F
         63
 CONSENSUS-G
                                                               64
 CONSENSUS-H
                                                               62
 CONSENSUS-0
 /<- nls ->/
 DESIGNED SEQ GSEELKSLYNTIATLMCVHQRIEVKDTKEALDKIEEEQKKSQQK......TQQAAA..DT.GS...SSKV
         TRFV
                                  ·VN K
 MUTATED AAS
E-ISOLATE
         GSEELKSLYNTIATLWCVHQRIEVKDTKEALDKIEEVQKKSQQKK.....QQAAA..DT.GS...SSKV
          g?eElkSlfNtvatLycvHqrIdvkDtKeAldkiEeignKskqk??????tqqaaA..?T.gs?..sskv
                                                              126
CONSENSUS-A
         128
CONSENSUS-B
                                                              120
CONSENSUS-C
                                                             125
CONSENSUS-D
         123
CONSENSUS-F
                                                             110
CONSENSUS-G
         -T--Q---LL-?-----?-?-?-?-??-??-????:...---T?.DK.??...??-?
-S??-?--N-AI?V-N---N-??I?--QQ-IQ-LK-V.M?-RKS...A-AAKE....--..?RQ?
CONSENSUS-H
                                                             106
                                                             106
CONSENSUS-0
CONSENSUS-CPZ ?S????----??V-W-?-??????--??-???K7????707?T-S---???G????-????-?????
                                                              61
           pl7 \/ p24
DESIGNED SEQ ....SQNYPIVQNAQGQMVHQPLSPRTLNAWVKVIEEKGFNPEVIPMFSALSEGATPQDLNMHLHIVGGH
MITATED AAS
                                V AS
         .... \texttt{SQNYPIVQNAQGQMVHQPLSPRTLNAWVKVIEEKGPNPEVIPMFSALSEGATPQDLNMMLNIVGGH}\\
E-ISOLATE
         ????SqNYPIVQNaqgOm?hQ?lSPrTLnAwVKviEekaFspEVIPmFsaLSEGATpQdLNmMLNiVgGH
                                                             190
CONSENSUS-A
         ....-v--ai----v------
                                                             194
CONSENSUS-B
         185
CONSENSUS-C
                                                             191
CONSENSUS-D
         ....-T----T----
CONSENSUS-F
         174
CONSENSUS-G
                                                             170
CONSENSUS-H
168
DESIGNED SEQ QAAMOMLKETINEEAAENDRVHPVHAGPIPPGOMREPRGSDIAGTTSTLQEQIGMMTN...NPPIPVGDI
                       1
                            VA I
MUTATED AAS
        QAAMOMLKETINEEAAENDRVHPVHAGPIPPGOMREPRGSDIAGTTSTLQEQIGMMTN...NPPIPVGDI
E-ISOLATE
         QAAMQMLKdtINeEAAewDr?HPVhAgPippgQmREPrGSDIAGtTStlqEqigwmTs...NPPiPVGdI
                                                             256
CONSENSUS-A
         261
CONSENSUS-B
                                                            251
CONSENSUS-C
                                                            257
CONSENSUS-D
CONSENSUS-F
         ------R-----R-----e-
                                                            239
CONSENSUS-G
         ----?-----A---?.,,--?----
                                                            233
CONSENSUS-H
         -G-L-V--EV----?--T--P??--L---I---T-----Q----?-T-R.??-??----
                                                            229
CONSENSUS-0
160
```

### FIGURE 3

MHR

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		p	24 \/ \/	'p2'	\/ p7		motif
MUTATED AAS	SILKALGTGATLEEMP T R P S	G G	V. V. CALARAMSQA	NN NN	-	R P V	N
ISOLATE-E	SILKALGTGATLEEMM	TACQGVGGPSHKAR	VLAEAMSQA .	QH.AN	.IMMQRGNP.	KGQTR.IKCF1	N
CONSENSUS-A	sILraLg?gAtLeEM	MTacOgVogPoHKA	rvLAEAmSov	a???n?	? iMmOrGof.	raakr?iKCI	FN 38
CONSENSUS-B	TKPa						
CONSENSUS-C	TPs			cn-5.a		Y-piv-	38
CONSENSUS-D	tKP?						
CONSENSUS-F	TKP			EII. 5 ° C.	a	K-Dryn-	·- · 38
CONSENSUS-G	T?P		a	INFG	KD	K-D33	? 36
CONSENSUS-H	??SI		э	3GA-A	4.:K::	K-Pff	
	QK?P?						
CONSENSUS-O	?K?	)	M:H:	MDPKGG I IV	.vrun.	P:R-G	
CONSENSUS-CPZ	;R;			r	<b>VF</b> ?-?-?G?	,-,,-u	- 26:
			pol cds				•
	Zn-motif ->/	/<-Zn-motif	->/ p7·	\\ 'r	o1, //	<b>p</b> 6	
DESIGNED SEQ O	CGKEGHLARNCRAPRKK I K	GCWKCGKEGHOMKI R	CT.E.ROAN			SKP R	
ISOLATE-E C	GKEGHLARNCRAPRKK	GCWKCGKEGHOMKD	CT.E.ROAN	s Flgkiwpsn	KG . RPGNFPOS	SKP	
CONSENSUS-A CONSENSUS-B CONSENSUS-C	CGREGHLARNCRAPEK				hi-	????????	453
	i-k						
	i-k						
	?						406
	I-?						. 411
CONSENSUS-CPZ	RR-	RQ?-;	-??-????V-	??-??	?-?V-	?????	306
	vpr binding				VDX	binding	p6
		•			_	+4	erminus
	/<>/		(minor)			<>/	/ (80%)
DESIGNED SEQ .	ЕРТАРРАЕ	NF.GFGEET	Г. PS РКС	EOKDi	(EHYPPSASI.K	ST.FCMDDT CO.	
MUTATED AAS		S R	Q	P	L L	S	
ISOLATE-E	БРТАРРАЕ	NW.GMGEE	••••••	.QKD	EHPPPSVSLK	SLPGNDPLSO	
	EPtAPpAE						
CONSENSUS-B ?	????e ???????	S- rf		gegka??	ke;;bb1;81)	(S1FGWDp1SQ	. 485
CONSENSUS-C ?	?????????	777770	-cps::::q-	pı	1Y?a1	:s	\$ 500
ONSENSUS-D	?????????		pa	·-p??	??t	x	479
ONSENSUS-F			Psq	??	lya		495
			. DC		1		482
CONSENSUS-H		(.????	?.?S	-P??	LY?	-	440
CONSENSUS-0	2-CM-	· · · · · S- · - F M-	P	-??	??	-	436
. 0-606140			וורם חלי	3 0 0			444
ONCOMOS-CPA .	I	Y.??Q?R	.??-?	????	??L?	?-??	333

CONSENSUS A-CPZ FROM LOS ALAMOS HIV SEQUENCE DATABASE ISOLATE-E SEQ FROM ISOLATE 93TH253 THAILAND

Underlined AA are not present in all overlapping segments

### FIGURE 3 (Cont)

DESIGNED SE	O FFRE.NLAFQOGKAREFSSEQTGANSSASRKLGDGGGAERQ P P R PT D	
MUTATED AAS		
ISOLATE-E	FFRE.NLAFQOGKAREFSSEQTGANSSASRKLGDGGGAERQ	
CONSENSUS-A	PPRE.NLAFQQGEAR?FSSEQT??NS?TSR?LWDGG?D??.L????G?E?Q	3
CONSENSUS-B	dp-ke-????????????Rap-r-B-gVw-r-nnS-S???-EA-adr	4:
ISOLATE-C	TX-EPRAP-TQV.RGSNT.FSEAGAERQ	46
CONSENSUS-D		35
CONSENSUS-0	PKEPRAPE-RVW-G-K.T-SET-A-R	48
CONSENSUS-U	PZ?????????LCA-?????????-???-?-?-???	13
COMSENSOS-C		
	protease	
PROTONED CEC	\/ <- gag cds end gctsssfsfpQitimQRplvtiKiGGQLKEALLDTGADDTvLeDinLpGKMKPKMIGGIGGPIKVRQYD	
MUTATED AAS	LN V I EM R	
ISOLATE-E	GTSSSPSFPQITLWQRPLVTIKIGGQLKEALLDTGADDTVLEDINLPGKWKPXMIGGIGGPIKVRQYD	
CONSENSUS-A	G???SF?PPQITLHQRPLVTV?I?GQLIEALLDTGADDTVLEDINLPGKNKPK?IGGIGGFIKVRQYD	96
CONSENSUS-B	tV-sik-gK	116
ISOLATE-C	TV-n	115
CONSENSUS-D	RA-??CLPDIA-VG-H-C-?NN-Q-E-?-?H	94
CONCENSIB-II	_ TV-SVRVGK	115
CONSENSUS-CP	2 ?-???-?-?-??????C??-?-?-?-Q-7?-?-?-??	55
	protease \/ p66, p51 QILIBICCKKAIGTVLVGPTPVNIIGRNMLTQIGCTLNFPISPIDTVPVKLKPCHDGPKVKQHPLTEBKI	
MUTATED AAS	I H L L R E	
MUINIED MC		
ISOLATE-E	QILIEICGKKAIGTVLVGPTPVNIIGRNMLTQIGCTLNFPISPIDTVFVKLKPCMDGPKVKQWPLTEEKI	
Consensus-à	QILIBICGKK?IGTVLVGPTPVNIIGRNMLTQIGCTLNFPISPIETVPVKLKP?MDGPKVKQMPLTEEKI	164
Consensus-B	н-А	186
isolate-c	I	184
CONSENSUS-D	NVTV-??-?EVQS?	159
Consensus-O Consensus-U		185
CONSENSUS-CP2	Z ?V?-?-??R?V??????L???G?GS?	106
	l was permit I wron	
	M41L D67N   K70R   KALTBICKEMEEEGKISKIGPENPYNTPVFAIKKKOSTKWRKLVDFRELNKRTODFWEVOLGIPHPAGLK	
MUTATED AAS	A T K R I	
	0	
ISOLATE-E	KALTEICKEMEEEGKISKIGPEN PYNTPVFAIKKKOSTKNRKLVDPRELNKRTODFWEVOLGIPHPAGLK	
CONSENSUS-A	KALT?IC?EMEKEGKISKIGPENPYNTPVFAIKKKOSTKNRKLVOPRELNKRTQOFWEVQLGIPH?AGLK	231
CONSENSUS-B	¥RT	256
SOLATE-C	AEQR	
CONSENSUS-D	B-7RI	254
Consensus-0	EAQQR	227
CONSENSUS-U	BW	255 164
CONSENSUS-CPZ	{	704
ESTGNED SEO	KKKSVTVLDVCDAYFSVPLDESFRKYTAPTIPSINNETPGIRYQYNVLPQGHKGSPAIFOSSMTKILEPF	
TUTATED AAS	ко т <u>Р</u> РО .	
	G	
SOLATE-E	kkksvtvldvgdayfsvpldesfrkytaftipsinnetpgiryqynvlpqghkgspaifqssmtkilepp	
CONSENSUS-A.	KKKSVTVLOVGDAYFSVPLD??FRKYTAFTIPS?NNETPG?RYQYNVLPQGWKGSP?1FQ?SMTKILEPF	295
CONSÉNSUS-B	kdiiA6	326
SOLATE-C	PSPO	334
CONSENSUS-D	eDIAS	324
CONSENSUS-O	0?0ASD	295
Consensus-u	EDIAS	325
CONSENSUS-CPZ	???????	225

polymerase motif

### FIGURE 4

DESTGNED SEC	QPIELPEKDSWTVNDIQKLVGKLNWASQIYAGIKVKQLCKLLRGTKALTDIVPLTEEAELELEENREI	•
MUTATED AAS	V E PRAET A	
MOINIED INCO	0	
ÍSOLATE-E	OPIBLPEKDSWIVNDIQKLVGKLNWASQIYAGIKVKQLCKLLRGTKALTDIVPLTEEABLELEENREI	
CONSENSUS-A	QP??LPEKDSWTVNDIQKLVGKLNWASQIYAGIK?KQLC?LLRGAKALTDIV?LTEEAELELAENREI	42
CONSENSUS-B	IvEvip	46
ISOLATE-C	IQTTT	
CONSENSUS-D	-sIkB	46
	-?10?-?V?QRV?EK-IT-SEV-P-S?E?	41
CONSENSUS-0	- In a second se	
CONSENSUS-U	IOD-EPVKPÀ	46
CONSENSUS-CP	Z -?I?????PI?-???-?-??-??-??	32
DESIGNED SEQ	.LREPVHGVYYDPSKDLVAEVQKQGQDQWTYQIYQEPFXNLKTGKYSRKRSAHTNDVRQLTEVVQKIATE	
:MUTATED AAS	K I I G F F(error) A M G K AA V	
ISOLATE-E	.LRIPVHGVYYDPSKOLVAEVQKQGQDQWTYQIYQEPFKNLKTGKYSRKRSAHTNDVRQLTEVVQKIATE	
CONSENSUS-A	.LK?PVHGVYYDP?KDLVAE?QKQGQDQWTYQIYQEPFKNLKTGKYA?KRSAHTNDVKQLTEVVQKV??E	484
CONSENSUS-B	e	533
!	BFSIINP-F	
ISOLATE-C	The bottom of th	531
CONSENSUS-D	ERm-G	
CONSENSUS-0		479
CONSENSUS-U	B	532
CONSENSUS-CP2	Z ???-???-???????-????-?	367
	p51 \/	
	SIVINGKTPKPRLPIQRETWETWHMEYWQATWIPEWEFVNTPPLVKLWYQLEKDPIVGAETFYVDGAASR  K K A TD B A V N	
mutated aas	K.K.A.TD BAV N	
ISOLATE-E	SIVIWGKTPKPRLPIQRETWETNUMEYWQATWIPEWEFVNTPPLVKLWYQLEKDPIVGABTFYVDGAASR	
CONSENSUS-A	SIVINGK?PKFRLPIQ?ETWE?WWMEYWQATWIPEWBFVNTPPLVKLNYQLEKDPI?GAETFYVDGAANR	550
CONSENSUS-B	ekktev	602
ISOLATE-C	TKATD	-
CONSENSUS-D	EI	600
	?-?L?VTRTA?SI??E?	541
CONSENSUS-O	TEV	602
Consensus-U Consensus-CP2		416
DESIGNED SEU RUTATED AAS	etkigkagyvidrgrokvisliettnoktelhaihlalqdsgsevnividsqyalgiiqaqpdrsesevv iv d q q l l k l	•
ISOLATE-E	etklgkagyvidrgrokvislietinoktelhaihlalodsgsevnividsqyalgiiqaqpdrsesevv	
ONSENSUS-A	ETK?GKAGYVTDRGRQXVVSLTETTNQKTELHAIHLALQDSGSEVNIVTDSQYALGIIQAQPDRSESE?V	618
ONSENSUS-B	1k1-	672
	I	
		670
ONSENSUS-D	L	
ONSENSUS-O	?LEQ-K-?IIK-?AM-?L?KB???-SSTQ-?-PI-	602
ONSENSUS-U	K	672
ONSENSUS-CPZ	;;;;-;;;;;;-;;OA:-;L;;;;;;;;;;;;	.459
	THE THE PROPERTY OF THE PROPER	
ESIGNED SEQ S	eqiieblikkekvylswypahkgiccneqvdklviscirkvlfldginkaqeeheryhsnnrtmasdfwl	
UTATED AAS 1	N K R A SA D K NE	
	Q .	
SOLATE-E	SOIIEBLIKKEKVYLSWYPAHKGIGGNEOVDKLVISGIRKVLFLDGINKAQEEHERYHSNWRTMASDFNL	
ONSENSUS-A	NOI I EKLI ? K? KVYLSWVPAHKGIGGNEQVDKLVS?GI RKVLFLOGI DKAQE?HB?YH?NW?AMASDFNL	681
ONSENSUS-B	sqK-EaeKsr	742
	QS-ER	
		244
	sQK-EA	740
onsensus-o	QE-TK-E?T	669
ONGENCIES-II	QQ-DEKSR	742
ONSENSUS-CPZ	????K?E?I	510
		•
ESIGNED SEQ F	PPIVAKEIVANCDROOLKGEAMHGOVDCSPGIWOLDCTHLEGKVILVAVHVASGYIEAEVIPAETGQETA	
UTATED AAS	PS IN I	
	С	

### FIGURE 4 (Cont)

ISOLATE-C	- 880 - 798 - 882
designed seq aehlktavomavfihnfkrkggiggysageriidiiatdiotkelokoitkionfrvyyrdsrdpiwkgp mutated aas $\underline{R}$ v s n l L	
ISOLATE-E AEHLKTAVQMAVPIHNPKRKGGIGGYSAGERIIDIIATDIQTKELQKQITKIQNPRVYYRDSRDPIWKGP	
CONSENSUS-A AEHLKTAVQMAVPIHNFKRKGGIGGYSAGERIIDIIA?DIQTKELQKQI?KIQNFRVYYRDSRDPIWKGI CONSENSUS-B	952
CONSENSUS-Diiiiiii	
CONSENSUS-O?	
CONSENSUS-UNTNNN	952
CONSENSUS-CPZ???T?-??-T???L-?-??	687
vif cds ->	
DESIGNED SEQ AKLLWKGEGAVVIODNSDIKVVPRRKAKIIRDYGKOMAGDDCVAGRODED	•
MUTATED AAS A S	
ISOLATE-E AKLLNKGEGAVVIQDNSDIKVVPRRKAKIIRDYGKQMAGDDCVAGRQDED	
CONSENSUS-A AKILMKGEGAVVIQDNSDIKVVPRRKAKIIRDYGKQMAGDDC?AGRQDED	929
CONSENSUS-B	1002
ISOLATE-CA-V	
MNGENCIC-DV-S	1000
CONSENSUS-O -QKGT-SM-NT-SESMEQPGEIP	925
CONSENSUS-UKHGTAW	1008
CONSENSUS-CPZ -?OGELV-SNKHGTAW	742
CONSENSUS A-CPZ FROM LOS ALAMOS HIV SEQUENCE DATABASE	
ISOLATE-C FROM GENBANK U46016 HIV-1 SUBTYPE C (ETHIOPIA)	
ISOLATE-E FROM GENBANK U51189 HIV-1 SUBTYPE E ISOLATE 93TH253 (THAILAND)	

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### <- pol cds

DESIGNED SEQ	MENRW.Q	. VMIVWQV L	DRMRIR K	TWNSLVKI K	н н Н	Kakgwp N	YRHHY F	esohf DR	KVSSE	VHIPLG	E D	RLVI I	
ISOLATE-E	MENRW.Q	. VMIVHQV	DRMRIR	TWNSLVK	HMYISK	KAKOWF	YRHHY	ESOHP	KVSSET	/HIPLG	EA	RLVI	
CONSENSUS-A	MENRW.C	O.VMIVWO	VDRMrI	RTWNSLVX	HHMYVS	KKAKGWI	FYRHH	f Esrh	pkvaSI	WHI PLA	3d	ARLVV	66
CONSENSUS-B	MENRW Q			k	i-	q		Yt-	-ri			i	. 66
ISOLATE-C	MENKW Q	ATTAMOA	DKMKTK	K		2D		/d-n-	T		-R		65
CONSENSUS-D		-7	2 OVU	KA	V-Y-2-	2-22N-2	>	rN	- -??	-YV	??	-??	54
CONSENSUS-O	z -????.?	· ??		??-?	?-1???	-3333-3	ì		???-	??7	????	?K-?-	34
DESIGNED SEQ	RTYMGI ()T	GEKDWOL	:HGVSII	EWROKRYS	TOVDPD	LADQLIH	ILQYFT	OCFSD:	STIRRA	ILGQIV	/RRR	CRYP	
MUTATED AAS	K H	RH	0	LS	G	H	Ħ	λ	A	HR	S	Q	
HOIMILD II-	••		_	K		_	<u>x</u>						
ISOLATE-E	RTYWGLQT	GEKDWQIA	Hevsi I	ewrokrys	TQIDPDI	ADQLIH	ILQYFI	CPSDS	STIRRA	ILGOVV	RRRC	CEYP	
CONSENSUS-A	RTYMGLH	TGEXDWHI	.GhGVS1	EWrgKRY:	STOVDPE	LADgLI	HLhyF	dCFSd	ISAIRK	AllGei	VRPF	(CBAO	136
CONSENSUS-B	t		-a	. <b>  </b>			y	е	n	n-	-s		136
ISOLATE-C	PTYNCI OT	CODMINIC	SUCCEST F	WPT.PSYN	MOVDEGI	ADHLIH	MHYFD	CPAES	:AIRKA	ILGYRV	SPRC	ЖĞ	
CONSENSUS-D	k		-0	102	G		-MY	E	7	h-	-5?-		132
CONSENSUS-0	7M	D78		?Y-?-I	(IE	TRM-		TT?	?	QR	-LTK	(?	118
CONSENSUS-CP2	T??-?-?	??		??G?-?	? <b>-</b> ?	T??-	-??	???	?-?-?	??	????	-3-K	76
					vpr	cds -	>			•		·	
DESIGNED SEQ	SCHNIKVGS	LOYLAL.	ALI	TPKKIRPE	LPSVKK	LTEDRWI	NKPQX	IKGHR	ENHTM	NGH			
	A	1	•	K K		K	B '	T R	G				
ISOLATE-E	SCHENIKVGS	LQYLAL.X	ALT	TPKRIRPE	LPSVKK	LTEDRN	NKPQK	I KCHR	en PTM	igh\$			
CONSENSUS-A	AGHNKVGS	SLOYLAL.	kal	VaPtkaKP	PLPSvk	ILL EDR	ne PQI	CTRGH	RGsR?	<b>м</b> дН\$			191
CONCENSUS - B			a	it-k-i	?		K	X	ht-				191
ISOLATE-C	ACIDIORCS	T JAIVO	AI. I	KPKKAKPP	LPSVSK	LVEDKN	VKPOX:	<b>TRGRR</b>	GNHTM	ich		•	
CONSENSUS-D	2		t i	i K - I	R		K	k'	?HT-				186
CONSENSUS-O	2507	r?	?-V	-K????	03	?	K???	?I-DQ!	L?~?S-				161
CONCENCIE CD2	2207		-7-777	?????R?	????		- K??F	2???-	RT : Ma	\			107

							•		
<b>:</b> .			<- vi	f cds			•	LR domain	1
•	/<-	,ol	igomeriza	tion	->,	/		/<-	
DESIGNED SEC	MEO.	AP EDOGPOREPY	NEWALELLE	ELKOEAVRH	PPRPWLHNLA	OYIYET	 YGDTWSGVEAI	LIRTLOOL	•
MUTATED AAs		SS	T	H	Ğ	Ħ	Ē	I	
				N	S		_	-	
ISOLATE-E	MEQ	AP EDQGPQREPY	vewalellei	elkqeavrhi	PRPWLHNL	OYIYET?	/gdtwsgveai	IRTLOOL	
CONSENSUS-A	ME?.	.AP.EDQGPQREP?	?E??LELLE	ELKHE?VRH	FPR?WLHGL	GQHIY?7	YGDTWEGV?A	IIRILQQL	58
CONSENSUS-B	q?	??y	N-Wt	?-A	i?-	E-	aE-		65
ISOLATE-C		AP EDOSSOREPYN							
CONSENSUS-D		Y							64
CONSENSUS-0	Q.	f	N-Wt	?-A	pa-	yE-	m-		66
CONSENSUS-U		H							. 67
CONSENSUS-CP	ZQ.	?-?	WT	-?-N-A	? <b>P</b> ?-???	?-???-?	-3333333-3	?????-??	33
		LR domain ->/	tat cds	->					
DESIGNED SEQ	мрін .	FRIGCOHSRIGIL	RORRA R	NGASRS					
MUTATED AAS	LV	$R \overline{I}$	G <sup>*</sup>	S					
		Ŧ							
ISOLATE-E	MFIH	PRIGCOHSRIGIL	RQRRA RI	NGASRS				•	
CONSENSUS-A	LF?H	FRIGCOHSRIGII.	?GRRG.F	enga?rs\$					84
CONSENSUS-B	i-3	?t.	ga?-	s					93
ISOLATE-C	LFVH I	PRIGCOHSRIGIF	AREKROE	isw					
Consensus-d	I	t.	RQA	SS					93
CONSENSUS-0		y??						•	94
CONSENSUS-U		T.							96
CONSENSUS-CPZ	??I	????-??L.	PQR.S	SN					54
4		•		•				٠.	
•									

	• •	
	intramolecular 3'sj 3'sj disulfide bonding \/ \/ }   rev cds ->/<- nls ->/	:
•		
DESIGNED SEQ	MDPVDPNLEPWNHPGSQPTTACSKCYCKKCCFHCQLCFLKKGLGISHGRKKR KQRRGAPQSRKDHQYP	•
MUTATED AAS	K K T Y V T Y R R SE	
1	. у	
ISOLATE-E	MELVDPNLEPWNHPGSQPTTACSKCYCKKCCWHCQLCFLKKGLGISHGRKKR KHRRGTPQSRKDHQYP	
CONSENSUS-A	M?PVDPnLEPWnHPGSqPtTaCskCYCK?CCwHCqlCFLnKGLGISYGrKKRr?RRgtPQs?kDhQnp	64
CONSENSUS-B	-erkktnkfvttQradSqtvs	68
CONSENSUS-C	?Kk-sYlVqt	65
CONSENSUS-D	-d	66
CONSENSUS-F	-ELD	68
CONSENSUS-O	-DE?PH?-O?P-NNRYYV???-???AAAP-?KD-	55
CONSENSUS-U	-DKKTKYPVPRSNSE	68
CONSENSUS-CP2	-D-?-????????-?-NNY??TK?-????T????S?NN-D?	45
e	xon \/ exon	
DECICNED CEO	I PEOPLPOTRGGNPTDPKESKKEVASKTETDPCD	
MUTATED AAS	S SP D GE KEA F	
isolaté-e	IPEQPLPIIRGGNPTDPKESKKEVASKAETDPCD	
CONSENSUS-A	ipKQplPqtqg??ptgpkESkKkVeSKteTDrf?\$	95
CONSENSUS-B	Ls?s-pr-DrEP?d?	99
CONSENSUS-C	-sr-dEp-D-	98
CONSENSUS-D	SS-pR-d?Ap-Dw\$	99
CONSENSUS-F	VIS-AR-NEA??-P?\$	96
CONSENSUS-O	V-?-S???-?RK.Q?RQE-QE??K??GP?G?P????SC??CTR?S?Q\$	83
CONSENSUS-U	SHRV.SEED-	. 101
	aa aa aaaaa aaaaakaa a aa aa aa aa aa aa	E2

	high-affinity binding site nls												
	\/ 3' sj		exon	\/	exon	/<-			->/ <sup>:</sup>				
DESIGNED SEC	MAGRSGSTDE EL	L RAVRI	INILYQ	SNP	YPSSEG	TROTE	KNRR	RRWRARQI	RQIRAI	SERI	LSTCL	GRS	
MUTATED AAS	D N	кі	K			S A	R	B	. HS	W	NĖ	P	
ISOLATE-E	magrsgstde el	L RAVRI	INILYQ	SNP	rpsseg	GTRQTR	INTR	rrwrarqi	RQIRAI	SERII	STCLG	:RS	
CONSENSUS-A	MAgRSG?sDE.el												66
CONSENSUS-B	d	<b>-tV-</b> ]	l£		p-s-e-	T	-R	e	r-	iw-	y-	s	67
ISOLATE-C	MAGRSGDSDE ELI	L KAVRI	KILYOS	NPY	PTPEG	TROAR	RNRRI	rrwraror	OIHTL	SERIL	SNPLG	RP	
CONSENSUS - F	N-?T	R-?-	<i></i>		B-	- T	-R		-?-R??	-?	s		61
CONSENSUS-O	BQ	200-			?-?-?-	N		R	A-V-?-	A?-?	-A-VV	HG?	56
CONSENSUS-U	DA	RVV			P-B-	.TT-			RA	P		S	67
CONSENSUS - CP	Z?E-??????	-??-VK-		?	?-?-	.?-?	-R-?-	??	?-????	??-V	-?-??		41
	Leu-r	ich					٠.						
	effector												
	/<-		•										
DESIGNED SEO	AEPVPLOLPPLERL	HLDCSED	CGTSGT	oos	CTETG	VGRPOI	SGES	SVILGPG	rkn				
TUTATED AAs			SD		•	-	Ē	AV S			•		
SOLATE-E	TEPVPLQLPPLERL	HLDCSED	CGTSGTC	)QSQ	GTETG	VGRPQI	SGES	SVILGPGT	MON				
CONSENSUS - A	AEPVPLQLPP1ERI	LhLDCsE	icgTSgT	<b>'Qq</b> ?	qq?et(	svGr <sub>P</sub> Q	vsVEs	ssavLGSG	Tkn				120
ONSENSUS-B		t?-		·.	?-	·s:	il	ъе	E\$				115
SOLATE-C	<b>AEPVPLQLPPLERLI</b>									)			
ONSENSUS - F	E?	?IN??	-E.Q-A	?E.		S7	T-G	H	E\$				105
ONSENSUS-0	O?NN?VDO-	?IRDP-?	D?L???	?TV	DPRAEL	NSCL-N	TLCSC	NT?????	???N\$				95
ONSENSUS-U													123
ONSENSIE - CDZ									- •				-23

						•			en <del>v</del> pho	phos	
DESIGNED SEQ	MTPL	EIIAI		LIIAIVV L		EYRKL	_	RIDRL K	IKRTRERA E I	EDSGNI	ES
MUTATED AAs			2.0		**		^	••			
CONSENSUS-A	mtPL???	eIcAl	vGLiV	ALILAIV	vwrivgi	. eyKk	llkgr	Ridr	l?ikRIrER	A.EDSgN	VES 5
CONSENSUS-B	-qs-	q-?	-a-v-	-a-i	Ē-	?r-:	i-R	?	d		50
ISOLATE-C	MVDLLAK	VDÝRIVI	VAFIV	ALIIAIV	VWTIAYI	EYRK	LLRQR	RIDRI	IKRTRERA	A EDSGN	IES
CONSENSUS - D	-0	v-1	-A-v-	i	£-	crr	-kr	w-	d	-?	57
CONSENSUS-F	-S??	LAIS?	TA	I	?Y-	R	R	N	.YE??		51
CONSENSUS-0	-H??	?LL-?	I??SA	L??INV?	?-? <b>F</b> ?	LR?	(-?-??Q	DR?E?E-LEF	LR?-IF	Z.DDY	42
CONSENSUS - U	-0	T-T	V-	-F-A	SY-	R-1	RK		.LD		57
CONSENSUS-CPZ	3??	?????	L????	??? <b>₩?-C</b> 3	(???I??	??-??}	Ж???	??????-?	.??1?????	. ??????	?- 14
DESIGNED SEQ	EGDTEE L	STM	VDM G	NYDLGVDI	INL						
MUTATED AAs	R	AL									
CONSENSUS-A	?GDT?E.	۱? <b>kL</b>	.VEM.	Snydlgvd	nNL\$						78
CONSENSUS - B	ege	-sa-???	??	H?apwdv	dD						79
ISOLATE-C .	DGDTEE L										
CONSENSUS - D	ErE										80
CONSENSUS-P	EAE										73
CONSENSUS-0	N?EE-QE										59
Consensus-u	DE										81
CONSENSUS - CPZ	-?EE??	-2?????	??????	PANP?.?	???DE		_				23

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<- vpU cds signal peptide / gpl20

		•	
DESIGNED SE	O MRVKETOMNNPNL WK	W GTLILGLVIIC SA SD NLWVTVYYGVPV	WRDADTTLFCAS
MUTATED AAS	R	M M M E	B T
CONSENSUS-A	Mrymoid?nyd?l wr??	.??W.gtmilq??iIc.na??e.?lWVtVyYGVP	/WkdaeTTI.fcAS
CONSENSUS - B		?lmlms	
CONSENSUS - C		ILGFwmlm,-vg.n	
CONSENSUS - D		?LmLMsv.a??	
Consensus - E		?sSd.N	
Consensus - P		LLFiLn	
CONSENSUS-G		LLVssn.n	
Consensus-o		?lylamALi-PLS??Q-YAs	
Consensus - u		???? ? ?? - ? -	
Consensus - Ce	2 -??????-???-?.???	??????-????.?T???	-??-?P??
	•	***	•
DESIGNED SEQ	DAKAHETEVHNVW ATHACVPTDP	POSTHLE NYTENFNMWINIMVEQMQEDVISLWD	QSLKPCVKLT
MUTATED AAS	YD	VV D D H I	
CONSENSUS-A	dakaydte?HNVW?aTHaCVPTDE	nPgEi?le.NVTE?FnmwkNnMVeQmheDiiSLW	).qSLkPCvkLt
XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX		vv-??n	-
CONSENSUS - C		шvndd	
ONSENSUS-D		N	
onsensus - e		qv	
ONSBNSUS-F	S-Ek-v	Vvn-dT	
ONSENSUS-G	ss		.E
ONSENSUS-O		?-?-yp-?dIYd	
ONSENSUS-U		????	
ONSENSUS-CP2	8 ?-???S????	?-??V????????-??-???????	?
	* *	^^^	
UTATED AAS ONSENSUS-A		YPERVARIABLE REGIONS 1/2	?
ONSENSUS-B			
INSENSUS-C			
INSENSUS-D			
INSENSUS-E		nvi-nvsniiq-it	
NSENSUS - P		t-?-?-q	
NSENSUS-G		?-?NcT?ennNstv-	?tLkE 1
NSENSUS-0	POMn- tel	-l	???
MSENSUS-U		?-?	
MSENSUS-CP2	^^ ^^		P???????
			•
Signed Seq Tated Aas	HYPERVARIABLE RE	GIONS 1/2	
NSENSUS-A	??eikNCsfNmTtelrdk)	tgkvysLfYrlDvVqi???????n??????	n????????? 10
NSENSUS-B		/e-akp-d?????	
SENSUS-C		Ai-pl	
NSENSUS-D		kq-hak	
		baki	_
nsensus-e nsensus-f		??HaI-p-s?	
		ktB-Akp-n?ss	
		E-KOAVs-L?k?N-tsT	
SENSUS-O		kt?-akP-nn	
		· · · · · · · · · · · · · · · · · · ·	
SENSUS-CPZ		????????-????	T 7
4	****		
	RLINCNTSVIKQACPKVSFOPIPIHY	CAPAGYAILKCNDKNFNGTGPCKNVSSVQCTHG	I KPVVSTQL
rated aas	S AT ITE	F NK T T	R

### FIGURE 10

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CONSENSUS-D CONSENSUS-E CONSENSUS-F CONSENSUS-G CONSENSUS-O CONSENSUS-U CONSENSUS-CI		234 254 245 251 228 205 120
DESIGNED SEC	LINGSLAEE EIIIRSENLTNNAKTIIVHLNESVEINCTRP NNNTR K HYPERVARIABLE REGIO	N 3/4/5
CONSENSUS - A CONSENSUS - B CONSENSUS - C CONSENSUS - D CONSENSUS - F CONSENSUS - F CONSENSUS - H CONSENSUS - O CONSENSUS - U CONSENSUS - U CONSENSUS - U CONSENSUS - C	LINGSLAe???v?irSenitnNaktiiVql??pV?InCtRP.nnntr.ks???vri???gpGq??afyae.e-vf-dnes-e?ihrte.iilvh-n-s-e-v?y?qxtp?l-t?e.EiIl	279 296 291 288 312 302 305 39 279 261
	otralization loop ->	
DESIGNED SEQ MUTATED AAS	HYPERVARIABLE REGION 3/4/5	
CONSENSUS - A CONSENSUS - B CONSENSUS - C CONSENSUS - D CONSENSUS - E CONSENSUS - F CONSENSUS - H CONSENSUS - H CONSENSUS - O CONSENSUS - U CONSENSUS - CP2	tgdi iG.dirqAhCnvsr?eWn?tlq?V a?qLr??f???nkt??iiP?n.ssGGD?-???i-ak-nkqi v-ke??qv-nq?	320 342 334 331 360 344 344 65 321 306 157
	J CD4	
DESIGNED SEQ MUTATED AAS	HYPERVARIABLE REGION 3/4/5	
CONSENSUS - A CONSENSUS - B CONSENSUS - C CONSENSUS - D CONSENSUS - F CONSENSUS - F CONSENSUS - G CONSENSUS - H CONSENSUS - O CONSENSUS - U CONSENSUS - CPZ	lEitthsPnCggef?FYCnts?lF.nstW???????       .n?t.???????????????????         pvm	355 374 366 361 398 372 373 92 356 336 175
	+ CD4   + ^^^   CD4 ^^^	
DESIGNED SEQ MUTATED AAS	HYPERVARIABLE REGION 3/4/5	
CONSENSUS - A CONSENSUS - B CONSENSUS - C CONSENSUS - D	tlq.CrI.kqIvnm.wQrvqq.AmYapPIq.g?irc?sNITGllLTRDGg??nns?????? -??-p	401 419 411 405

### FIGURE 10 (Cont)

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	^^^				gp120	/ gp41		
						VG IGA	MI PODI CA	
DESIGNED SE				VAPTR AKRRV	V EREKKU O	VG IGA L	FL	
MUTATED AAS	I MMR		E K	I K	V		r D	
	?net FrPgGgdm	-AND-CELVE	YKwVkieDl	CvaDrr akrDV	rveREXX	A??va.1G	evfloflGa	462
CONSENSUS-A	-t-i	[CMMT SPD1/		k		?i-	-m	480
CONSENSUS-B	-?		p-k	?.	-??	?i-		470
CONSENSUS-C CONSENSUS-D			r	· ?		I	m	465
CONSENSUS-E	Ni	K	0	·i		:1	Mif	508
CONSENSUS-F	-2n-l	k	e	a-	k	?	1	478
CONSENSUS-G			k	R	G	?		481
CONSENSUS-H	-?V		??	???	?	<b></b> ?-		187
CONSENSUS-0	?-1?	t-I7f	rvx-F	ki-RP?I	gt?t?H	<b>-</b>	Lv-S-	462
CONSENSUS-U	_?			??	?	<b>M</b>	?	435
CONSENSUS-CE	Z -?????-?????	?-????-	-77-75	???R???	????.?-Q	??:?-?	?? <b>-</b> ?-	227
		•						
DESIGNED SEC	AGSTMGAASITLT	<i>i</i> qarqllsgiv	/QQQSNLLR/	I EAQOHLLOLT	vngi koloar	<i>IL</i> AVERYLK	D QKPLG	
MUTATED AAS	Ж	L .	·N	Ħ		Ţ	QΓ	
						LANGE BANKS	-D 0011C	E27
CONSENSUS-A	<b>AGSTINGAASITL</b> T	<b>vQargLlSGI</b>	VqqQsN11r	AleaOghliki.	LAMCI KATAN	CALMARITE	ED.QQUIA	531 548
CONSENSUS-B			n	q		i	K	539
CONSENSUS-C			N	<del></del>			k	533
CONSENSUS-D							KKE	577
CONSENSUS-E			n					546
CONSENSUS-P CONSENSUS-G		V					?	549
CONSENSUS-H			?	??				227
CONSENSUS-0	AT3	+h+-?K	p	O?R-S	RR	LL-Tli(	Nn	529
CONSENSUS-U		??-??	N	0		<u></u> }	:S	496
CONSENSUS-CP	z???	?-?-?-??	??	?Q-S	:?V	???	? <del>-?-?</del>	279
			•		**			
	• •	~~~						
•		<b>_</b>		LEEIWNNHTWM	PUPPET CHYT	NOTYP TI.T	TECNÍAA ·	
	LWGCSGKIICTTAV		SNK			SL K	220100	
mutated aas	I F M	T		P D 1	<b>U</b>	3 <b>5</b> A	•	
	INGCSGKLICETO	TOWN CH	s m	รวรส์ไ <b>ฟิสกศาพ</b>	lowdkrisny	r?iIY?.Li	EesangO	586
CONSENSUS-A			-7	-1-??	me-erd	lt		603
CONSENSUS-B CONSENSUS-C				-0	mr	-dtr?-L	-d	597
CONSENSUS-D	b		<del> T</del>	-L-e?	nE-ERd	-G18	?	589
CONSENSUS-E	I	t	<del>-</del> . <del>- x</del>	-feen	iB-eR	-Nqe.IL	T	636
CONSENSUS-P	7		<del>-</del>	-aBe?	4E-e	:neR	-?	603
CONSENSUS-G		t	<del>-</del> . <del></del>	-fnE	[e-eRN	qnl	?	606
CONSENSUS-0	LXY-S-	K?t-?G	??	?neS?L(	3dd-u-v:	:s?e.e-	D?A-?	580
CONSENSUS-U	LT-		:::::::::::::::::::::::::::::::::::::::	-LVTLL}	4ER	QVGL	-DK	555 312
CONSENSUS-CPZ	L??-??-?-T-	N????	???????.??	?? <u>?</u> -?(	);;PA:-:.	6:-::0	::A::	312
							\/ 3'sj	
							.,,	
PROYEMED CEV	DRNEQELLELOKWAS	T. NAME TO T THE	I.MYTKTPIH	IVGGLIGLRIVE	PAVLSIVNRV	OGYSPLSF	<b>OTLLPA</b>	
MUTATED AAS	KD A	N SK	D 2 ZNZ1 2	V I	I		T	
MUIAIED AAS	•							
CONSENSUS-A	E)(NEqdLLaLDkWa	nLwnWPdIsn	WLWYIriPi:	nIVGGLIGLRIV	faVlsiInRV	RqGYSP1S1	Qtltp?	655
CONSENSUS-B		e?-t-	<b>k</b>	V	<b>V</b>		;1-a	671
CONSENSUS-C	b	7-+7	<b>: b</b>	<i>-</i> i	V		n	664
CONSENSUS-D		SS-T?	k		1V		1-a	657
CONSENSUS-E	DD TP	ST-	K	i	V		р?нп	705
CONSENSUS-F		S	K		V	-K3	hi-S	672
CONSENSUS-G	?	5ss		k	V		SHH	674
CONSENSUS-0	K?EE	SilTK	K-A-1	Av-Vi	mi – - nivkni	01	-1533V	647
CONTORNICHE - 17	S-KE	SG-T-	K		-T-F		D-T	625
CONSENSUS-CPZ	-?-???-?E?-?	ST?	K?-	??1??	????-??R?-	??	-2222-	355
4	<- tat	cds		•				
					VUDI PATTI	A AD TIM	T.I.CHE	
	PRG PDRPEGIEEEG	G EQURDRSV		WUULKSLCLIS	L AHKTKOPIPI	V T	R	
MUTATED AAS	LGR	rg <u>g</u>	n s	B	•	•		

### FIGURE 10 (Cont)

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CONSENSUS-U		. адт-6-т													702
Comsensus-U		G-T													685
CONSENSUS-CI	PZ Q?-	. ?????B-	?-??	??- <sup>°</sup>	???-?	?-??	?-?-		N-GIW-	-QS-TS	LACN	.v.w	-##L#	TL	398
								rev	cde						
							•	100							
DESIGNED SEC	SLRG	LRRG ·	WEAL	KYL W	4LLQY	WGQEI	KIS.	AVSL	LNATAI	AVAEGT	DRVI	EVAQ	RAGRA	ILHI	
MUTATED AAs	K	Q	G	WG	F	L	N	1		GW	I	v	W	N	
CONSENSUS-A	slkg	ılrlg	weg	lkyl.	MLlly	MgrE	LK?	SAinl	ldtiA	iavAqw	tDRv:	(Eig(	rigR	Ailnı	780
CONSENSUS-B		.??													789
CONSENSUS - C	r-	-gr	a-	·G	s-vq-	·ī-	k-	s-		EG	i-	??-	?	?	787
CONSENSUS - D		R	a-	<u>-</u>	q-	-?q-	n-	5-		Eq-	?-	-?v-	-a?	v-h-	773
CONSENSUS-B		R													832
CONSENSUS-P		~-R													787
CONSENSUS-G															800
CONSENSUS-O	lI?y	-gLHII	GQkt I ea	CR-c?	Av?Q-	-LQ	- an -	-T	?-V	N	-qi-	lGi-	?0		767
CONSENSUS-U		R	A-	G	v	0	- N-	s-	-NAT	VEG-	I-	-v	C		741
CONSENSUS-CP		L													460
· · · · · · · · · · · · · · · · · · ·															
DESIGNED SEQ		QGLERALL											•		
MUTATED AAs	T	P													
CONSENSUS - A	PrRII	QGlEraL	\$												793
CONSENSUS-B	-?		-											•	801
CONSENSUS - C		F-aq	r-												BDO
CONSENSUS-D															785
CONSENSUS - E														•	. 845
ONSENSUS - P	-?	?	-												798
ONSENSUS-G															813
ONSENSUS-O		?												•	779
ONSENSUS-U		F	-												754
ONSENSUS-CP2															473

DECICNED SE	Q MGGKWSKSSLVGW	PEVRERIROT	PPAAEC	VGAVSQD	LDXHGAITSSNTPA	
MUTATED AAS		A RA	А	AR	Y L A	
MUINIED ANS	• •				_	
TOOT BOD. P	MGGKNSKSSIVGN	POVERRIKOT	PPAAEG	VGAVSQD	LDICHGAVTSSNM	
ISOLATE-E	FIGGRADADS I VON	I MANDON TONE -		_		
	MCCANGAG I NON	Tourdayuag	?PtAAkG	VGAVSOD	.LDkhGAiTSSNt??	48
CONSENSUS-A	AGGKHSKSSIVGH	20 x3222	?????????-Epd-	T	eaa	46
CONSENSUS-B			ADAREC	VGAASRD	LDKYGALTSSNTPA	••
ISOLATE-C	MGGTMSKCSPVGW	PAIKEKIKKA	??dPD-	P-		50
CONSENSUS-D		-WI-K-I-I-222	7	K	-73D-G-3K-DO	38
CONSENSUS-0	NA??-?KF?	???R?	???P?-?PC-P-	::-KE	A:K-G-:N-PQ	31
CONSENSUS-U	7?????	-??-E-I-?-???.	P???-	?::::		31
\vskip6pt			1 1 11 11			
	* SH3	-binding	SH3-binding	3,		
					WCFFDOETI DI ATT	
DESIGNED SEC	NNADCVWLK AQB		POVPLRPMTYKGAFDLS			
MUTATED AAs	PAE	В	A V I	L D	I Q D	
ISOLATE-B	NNADCVNLR AGE	E EG VGFPVR	POVPLRPMTYKGAFDLS1	PLKEKGGLEG	PAASKKKORITOFMA	
CONSENSUS-A	tnpsCaWLE?Aqe?	.de?.VGPPVR	POVPLRPHTYK9AvDLS1	PLKRKGGTDG	TÄZSKKORTEDEMA	110
CONSENSUS-B	ad	.e??-e?	a-?	е	-?-qa	108
ISOLATE-C	NNPDCAWLE AGEE	E EE VGFPVR	POVPLRPMTYKAAFDLSI	.PLKEKGGLEGI	.IYSKKRQEILDLWV	
CONSENSUS-D	d	RS - E	e	E	-W-X	115
CONSENSUS-O	N-AAT P-? . SH? .	. ? ?	PP	·?-·	HA?	93
CONSENSUS-U	N-??-?????	.E?E	???		??	83
\vskip6pt	•					• _
•			SH3-binding		•	•
		•	.		• . •	
DESIGNED SEQ	YHTOGFFPDWHNYT	PGPGIRY PLTFG	CFKLVPVDPREVE BIN	RGENNCLLHEM	SOUCHEDEEKEAPI	
	YHTOGFFPDWHNYT	PGPGIRY PLTFG) T	CPKLVPVDPREVE BIN S A	RGENNCLLHUM I	CP D K	
DESIGNED SEQ	M Ā O	T V	S A	B I	CT D K	
	M Ā O	T V	CPKLVPVDPREVE EIN S A	B I	CT D K	
MUTATED AAS	N A O	T V PGPGIRY PLCFG	S A	e i Kcenncllhpm	SOHGIEDEEREVLI	
MUTATED AAS	N Y Q  YHTOGFFPDWDNYTI  YNTOGFFPDWONYTI	T V PGPGIRY PLCFGM PGPGTRf.PLTFGM	S A : CCPKLVPVDPREVE EDNI CCFKLVPvDPaEVR.eat	e i Kgenncllhpm Pgennsllhpi	CL D K SQHGIEDEEREVLI CQHGmdDe?revLm	176
MUTATED AAS ISOLATE-E CONSENSUS-A	N Y O  YHTOGEFPDWONYTI	T V PGPGIRY PLCFGM PGPGtRf.PLTFGM	S A : CCPKLVPVDPREVE EDN CCFKLVPvDPaEVR.eate-ekn	E I KGENNCLLHPM PGENNSLLHPI	CL D K SQHGIEDEEREVLI CQHGmdDe?revLm s1pB?	176 174
ISOLATE-E CONSENSUS-A CONSENSUS-B	M Y Q  YHTOGFPPDMHNYTI  YNTOGFFPDMONYTI  -hy	T V PGPGIRY PLCFGW PGPGtRf.PLTFGW	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPaEVE .eat: CFKLVPVDPSEVE EIN	E I KGENNCLLHPM PGENNSLLHPI BEGENNCLLHPA	CL D K SQHGIEDEEREVLI CQHSmdDe?revLm s1pE? SLHGMEDEDREVLK	
ISOLATE-E CONSENSUS-A CONSENSUS-B ISOLATE-C	M Y Q  YHTOGFPPDMHNYTI  YNTOGFFPDMONYTI  -hy	T V PGPGIRY PLCFGW PGPGtRf.PLTFGW	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPaEVE .eat: CFKLVPVDPSEVE EIN	E I KGENNCLLHPM PGENNSLLHPI BEGENNCLLHPA	CL D K SQHGIEDEEREVLI CQHSmdDe?revLm s1pE? SLHGMEDEDREVLK	
ISOLATE-E  CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D	YHTOGFPPDWDNYTI -hy	T V PGPGIRY PLCFGN PGPGERF.PLTFGN	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVR.eat: CFKLVPVDPSEVE EIN! L	E I  KGENNCLLHPM PGENNSLLHPI  GGENNCLLHPA  3t-c?  72A?A	CL D K SQHGIEDEEREVLI CQHGmdDe?revLm slpB SLHGMEDEDREVLKE-pE-qk -??B-?H?-I-?	174
MUTATED AAS  ISOLATE-E  CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-O	YHTOGFPPDWDNYTI -hy	T V PGPGIRY PLCFGN PGPGERF.PLTFGN	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVR.eat: CFKLVPVDPSEVE EIN! L	E I  KGENNCLLHPM PGENNSLLHPI  GGENNCLLHPA  3t-c?  72A?A	CL D K SQHGIEDEEREVLI CQHGmdDe?revLm slpB SLHGMEDEDREVLKE-pE-qk -??B-?H?-I-?	174
ISOLATE-E  CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D	YHTOGFPPDWDNYTI -hy	T V PGPGIRY PLCFGN PGPGERF.PLTFGN	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVE.eate-ekng	E I  KGENNCLLHPM PGENNSLLHPI  GGENNCLLHPA  3t-c?  72A?A	CL D K SQHGIEDEEREVLI CQHGmdDe?revLm slpB sLHGMEDEDREVLKE-pE-qk -??E-?H?-I-?	174 182 150
ISOLATE-E CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-D CONSENSUS-O CONSENSUS-U	YHTOGFPPDWDNYTI -hy	T V PGPGIRY PLCFGN PGPGERF.PLTFGN	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVR.eat: CFKLVPVDPSEVE EIN! L	E I  KGENNCLLHPM PGENNSLLHPI  GGENNCLLHPA  3t-c?  72A?A	CL D K SQHGIEDEEREVLI CQHGmdDe?revLm slpB sLHGMEDEDREVLKE-pE-qk -??E-?H?-I-?	174 182 150
MUTATED AAS  ISOLATE-E  CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-O	YHTOGFPPDWDNYTI -hy	T V PGPGIRY PLCFGN PGPGERF.PLTFGN	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVR.eat: CFKLVPVDPSEVE EIN! L	E I  KGENNCLLHPM PGENNSLLHPI  GGENNCLLHPA  3t-c?  72A?A	CL D K SQHGIEDEEREVLI CQHGmdDe?revLm slpB sLHGMEDEDREVLKE-pE-qk -??E-?H?-I-?	174 182 150
ISOLATE-E CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-D CONSENSUS-O CONSENSUS-U	YHTOGFPPDWDNYTI -hy	T V PGPGIRY PLCFGN PGPGERF.PLTFGN	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVR.eat: CFKLVPVDPSEVE EIN! L	E I  KGENNCLLHPM PGENNSLLHPI  GGENNCLLHPA  3t-c?  72A?A	CL D K SQHGIEDEEREVLI CQHGmdDe?revLm slpB sLHGMEDEDREVLKE-pE-qk -??E-?H?-I-?	174 182 150
ISOLATE-E CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-D CONSENSUS-U \vskip6pt	M Y Q  YHTQGFPPDWHNYTI  'hy YMTQGFFPDWQNYTI	T V PGPGIRY PLCFGN PGPGERF.PLTFGN	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVR.eat: CFKLVPVDPSEVE EIN! L	E I  KGENNCLLHPM PGENNSLLHPI  GGENNCLLHPA  3t-c?  72A?A	CL D K SQHGIEDEEREVLI CQHGmdDe?revLm slpB sLHGMEDEDREVLKE-pE-qk -??E-?H?-I-?	174 182 150
MUTATED AAS  ISOLATE-E  CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-D CONSENSUS-U  \vskip6pt  DESIGNED SEQ	M Y Q  YHTQGFPPDMHNYTI  YNTQGFPPDMQNYTI  -hy	T V PGPGIRY PLCFGN PGPGERE.PLTFGN	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVR.eat: CFKLVPVDPSEVE EIN! L	E I  KGENNCLLHPM PGENNSLLHPI  GGENNCLLHPA  3t-c?  72A?A	CL D K SQHGIEDEEREVLI CQHGmdDe?revLm slpB sLHGMEDEDREVLKE-pE-qk -??E-?H?-I-?	174 182 150
ISOLATE-E CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-D CONSENSUS-U \vskip6pt	M Y Q  YHTQGFPPDWHNYTI  'hy YMTQGFFPDWQNYTI	T V PGPGIRY PLCFGN PGPGERF.PLTFGN	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVR.eat: CFKLVPVDPSEVE EIN! L	E I  KGENNCLLHPM PGENNSLLHPI  GGENNCLLHPA  3t-c?  72A?A	CL D K SQHGIEDEEREVLI CQHGmdDe?revLm slpB sLHGMEDEDREVLKE-pE-qk -??E-?H?-I-?	174 182 150
MUTATED AAS  ISOLATE-E  CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-O CONSENSUS-O CONSENSUS-U  \vskip6pt  DESIGNED SEQ MUTATED AAS	YHTOGFPPDWHNYTI YMTOGFPPDWONYTI -hy YMTOGFPDWONYTI	T V PGPGIRY PLCFGN PGPGERF. PLTFGN	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVR.eat: CFKLVPVDPSEVE EIN! L	E I  KGENNCLLHPM PGENNSLLHPI  GGENNCLLHPA  3t-c?  72A?A	CL D K SQHGIEDEEREVLI CQHGmdDe?revLm slpB sLHGMEDEDREVLKE-pE-qk -??E-?H?-I-?	174 182 150
MUTATED AAS  ISOLATE-E  CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-D CONSENSUS-U  \vskip6pt  DESIGNED SEQ	M Y Q  YHTQGFPPDMHNYTI  YNTQGFPPDMQNYTI  -hy	T V PGPGIRY PLCFGN PGPGERF. PLTFGN	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVR.eat: CFKLVPVDPSEVE EIN! L	E I  KGENNCLLHPM PGENNSLLHPI  GGENNCLLHPA  3t-c?  72A?A	CL D K SQHGIEDEEREVLI CQHGmdDe?revLm slpB sLHGMEDEDREVLKE-pE-qk -??E-?H?-I-?	174 182 150
MUTATED AAS  ISOLATE-E  CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-O CONSENSUS-U  \vskip6pt  DESIGNED SEQ MUTATED AAS ISOLATE-B	M Y Q  YHTQGFPPDMHNYTI  'hTQGFPPDMQNYTI  'hy  YNTQGFPPDMQNYTI	T V PGPGIRY PLCFGN PGPGERF.PLTFGN	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVR.eat: CFKLVPVDPSEVE EIN! L	E I  KGENNCLLHPM PGENNSLLHPI  GGENNCLLHPA  3t-c?  72A?A	CL D K SQHGIEDEEREVLI CQHGmdDe?revLm slpB sLHGMEDEDREVLKE-pE-qk -??E-?H?-I-?	174 182 150 138
MUTATED AAS  ISOLATE-E  CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-O CONSENSUS-O CONSENSUS-U  \VSkip6pt  DESIGNED SEQ MUTATED AAS ISOLATE-B CONSENSUS-A	YHTOGFPPDWHNYTH YMTOGFPPDWONYTH -hy YMTOGFPPDWONYTH	T V PGPGIRY PLCFGM PGPGERÉ.PLTFGM	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVE.eat: CCFKLVPVDPSEVE EINIeq	E I  KGENNCLLHPH  PGENNSLLHPI  EGENNCLLHPA  3t-c?  F7-7A?A	CL D K SCHGIEDEEREVLI CCHGMCDe?revLm s1? SCHGMEDEDREVLKE-pE-qk?E-?H?-I-?	174 182 150 138
MUTATED AAS  ISOLATE-E  CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-O CONSENSUS-U  VERLIPEPT  DESIGNED SEQ MUTATED AAS ISOLATE-B CONSENSUS-A CONSENSUS-B	YHTOGFPPDWHNYTH  YMTOGFPPDWONYTH  -hy	T V PGPGIRY PLCFGN PGPGERÉ.PLTFGN	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVR.eat: CFKLVPVDPSEVE EIN! L	E I  KGENNCLLHPH  PGENNSLLHPI  EGENNCLLHPA  3t-c?  F7-7A?A	CL D K SCHGIEDEEREVLI CCHGMCDe?revLm s1? SCHGMEDEDREVLKE-pE-qk?E-?H?-I-?	174 182 150 138
MUTATED AAS  ISOLATE-E  CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-O CONSENSUS-O CONSENSUS-U  \VSkip6pt  DESIGNED SEQ MUTATED AAS ISOLATE-B CONSENSUS-A	YHTOGFPPDWHNYTH  YNTOGFPPDWONYTH	T V PGPGIRY PLCFGN PGPGVRY PLTFGN	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVE.eat: CCFKLVPVDPSEVE EINIeq	E I  KGENNCLLHPH  PGENNSLLHPI  EGENNCLLHPA  3t-c?  F7-7A?A	CL D K SCHGIEDEEREVLI CCHGMCDe?revLm s1? SCHGMEDEDREVLKE-pE-qk?E-?H?-I-?	174 182 150 138
MUTATED AAS  ISOLATE-E  CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-O CONSENSUS-U  VERLIPEPT  DESIGNED SEQ MUTATED AAS ISOLATE-B CONSENSUS-A CONSENSUS-B	YHTOGFPPDWHNYTH  YMTOGFPPDWONYTH  -hy	T V PGPGIRY PLCFGN PGPGVRY PLTFGN	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVE.eat: CCFKLVPVDPSEVE EINIeq	E I  KGENNCLLHPH  PGENNSLLHPI  EGENNCLLHPA  3t-c?  F7-7A?A	CL D K SCHGIEDEEREVLI CCHGMCDe?revLm s1? SCHGMEDEDREVLKE-pE-qk?E-?H?-I-?	174 182 150 138 199 230
MUTATED AAS  ISOLATE-E  CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-O CONSENSUS-U  VERLIPEPT  DESIGNED SEQ MUTATED AAS ISOLATE-B CONSENSUS-A CONSENSUS-B ISOLATE-C	YHTOGFPPDWHNYTH  YNTOGFPPDWONYTH	T V PGPGIRY PLCFGN PGPGVRY PLTFGN	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVE.eat: CCFKLVPVDPSEVE EINIeq	E I  KGENNCLLHPH  PGENNSLLHPI  EGENNCLLHPA  3t-c?  F7-7A?A	CL D K SCHGIEDEEREVLI CCHGMCDe?revLm s1? SCHGMEDEDREVLKE-pE-qk?E-?H?-I-?	174 182 150 138 199 230 206 166
MUTATED AAS  ISOLATE-E  CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D CONSENSUS-O CONSENSUS-U  VERLIPEPT  DESIGNED SEQ MUTATED AAS ISOLATE-B CONSENSUS-A CONSENSUS-B ISOLATE-C CONSENSUS-D	M Y Q  YHTQGFPPDMHNYTI  'AnTQGFPPDMQNYTI  -hy	T V PGPGIRY PLCFGN PGPGRF. PLTFGN	S A : CCPKLVPVDPREVE EDN! CCFKLVPVDPAEVE.eat: CCFKLVPVDPSEVE EINIeq	E I  KGENNCLLHPH  PGENNSLLHPI  EGENNCLLHPA  3t-c?  F7-7A?A	CL D K SCHGIEDEEREVLI CCHGMCDe?revLm s1? SCHGMEDEDREVLKE-pE-qk?E-?H?-I-?	174 182 150 138 199 230

### FIGURE 11

GAG OVERLAPPING SEGMENTS

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FIGURE 12 (Cont)

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Segment 18	Segment 19	Segment 20	Segment 21	Segment 22	Segment 23
IPVGDIYKRWIILGLNKIVRMYQPVSILDI V rtt occ gig ggc gaw atc tat aag aga tg att cig gga ctc aac aaa atc gig aga atg tat yma ccc gic agc att cig gat atc	NKIVRMYOPVSILDIRQGPKEPFRDYVDRF S aat aag att gtc agg atg tac yma cct ctc tcc atc ctc gac att arg caa ggc cct aag gaa ccc ttt agg gat tac gtc gac aga ttc	ROGPKEPFRDYVDRFYKTLRAEQATOOFKN K ara cag gga ccc aaa gag cct ttc aga gac tat gtg gat agg ttt twc aaa acc ctc agg gct gag caa gcc wca cag gaw gtg aaa aac	YKTLRAEQATQEVKNWMTETLVONANPDC F twt ang aca etg aga gcc gaa cag gct wee caa gas gtc ang aat tgg atg ace gas aca etg etc gtg caa aac gct aac eet gae tgt	WMTETLLVQNANPDCKSILKALGTGATLEE  D TRP S tgg atg aca gaw acc etc etg gtc cag aat gcc aat ccc gat tgc aag wcc atc etc arg get etg gga mcc gga gcc wca etg gaa gag	KSILKALGTGATLEEMMTACOGVGGPSHKA TRPS Assa were att etg ara gee ete gge mea gge get wee ete gag gaa atg atg aca gee teg ega gtg gga gge eet rge eat aag get

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Segment 24	Segment 25	Segment 26	Segment 27	Segment 28	Segment 29
MMTACQGVGGPSHKARVLAEAMSQATHANIS G atgatgacc get tgc caa ggc gtc ggc gga ccc rgt cac aaa gcc agg gtc etg gca gag gct atg tcc cag gyg amc mac gct aac att	RVLAEAMSQATHANIMMQRGNFKGQKRIIK Saga gg ctc. gcc gaa gcc atg agc caa gyc amc mat gcc aat atc atg atg cag agc caa gyc amc mat gcc aat atc atg atg cag aga ggc aat ttc ara ggc cma aag aga atc rtc aaa	MMQRGNFKGQKRIIKCFNCGKEGHLARNCR RPV atg atg caa agg gga aac tit arg gga cmg aaa agg att ric aag tgc tit aac tgt gga aag gaa ggc cat mic gct arg aat tgc aga	CFNCGKEGHLARNCRAPRKKGCWKCGKEGH IK tgt ttc aat tgc ggc aaa gag gga cac mtt gcc ara aac tgt agg gcc cct aga aag aaa ggc tgt tgg aaa tgc gga arg gaa ggc cat	APRKKGCWKCGKEGHQMKDCTERQANFLGK R gct ccc agg aam aag gga tgc tgg aag tgt ggc ara gag gga cac cag atg aag gat tgc aca gag aga cag gct aac ttt ctg gga aag	OMKDCTEROANFLGKIWPSNKGRPGNFPQS  H  S  Caa atg aas gac tgt acc gaa agg caa ttc ctc ggc aaa atc tgg ccc tcc mrc aaa ggc aga ccc gga aac ttt cyc caa agc

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Segment 30		Segment 31	Segment 32	Segment 33
P T. A P P A E N F G F G	ggc aat tte eyg cag tee arg eet gag eet ace get eee eet gee gaa are ttt rga tte gge	ENFGFGEETTPSPKQEQKDKE SR gag art ttc rgg ttc gga gag gaa acc aca ccc tcc cma aag caa gag cma aag gat aag gag	r gac	
臼	tec arg cet gag cet ace get e	GERTTPSP Q gga gag gaa acc aca ccc tcc c	QKDKEHYPPSASLKSLFGN PLL	SLFGNDPLSQ S age ete tte gga aac gat ece tya tee caa
0 N F P O S K F L C R P P	at tto cyg cag t	ENFGFG SR gag art ttc rgg ttc gg	EOKDKE P	S L F G N D
ය 다	gga agg cet gge a	PPAEN S	D E O E O Cmg saa cag gaa	S L K S L
В В В В В В В В В	tgg cet age mre aag g	PEPTAI	T T P S	Y P P S A S L
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POL OVERLAPPING SEGMENTS

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Segment 1	Segment 2	Segment 3	Segment 4	Segment 5	Segment 6
FFRENLAFQQGKAREFSSEQTGANSSASKK ttc ttt agg gaa amc ctg gct ttc cmg caa ggc raa gcc aga gag ttt ycc agc gaa cag aca raa gcc aga gag ttt ycc agc gaa cag aca raa gcc raa gcc aga gag ttt ycc agc gaa cag aca raa gcc raa gcc aga gag ttt ycc agc gaa cag aca raa gcc raa gcc aga gag ttt ycc agc gaa cag aca raa gcc raa gcc raa gcc aga gag ttt ycc agc gaa cag aca raa gcc raa gaa tt ycc agc gaa cag aca raa gca raa gcc raa	TGANSSASR R PT  A aca rgg gct aac tcc yct rca agc aga	SFPOITLWOI	t cag att acc ctc tgg cag aga ccc ctc gtg acartc aaa	and att 99a 99c can ct9 awa gaa  DDTVLEDT	a 9tg ctc

Segment 13		Segment 14		Segment 15		Segment 16		Segment 17	
LTEICKEMEEEGKISKIGPENPYNTPVFAI A T K R R I I I I I I I I I I I I I I I I I	ctc acc gmg atc tgt ama gaa atg gaa vaa gaa ggc aaa atc tcc arg att ggc cct gag aat ccc tat aac aca ccc rtc tt gcc att	KIGPENPYNTPVFAIKKKDSTKWRKLVDFR R	arg atc gga ccc gaa aac cct tac aat acc cct rtc ttc gct atc aag aaa aag gac tcc acc aaa tgg aga aag ctc gtg gat ttc aga	KKKDSTKWRKLVDFRELNKRTQDFWEVQLG	aaa aag aaa gat agc aca aag tgg agg aaa ctg gtc gac ttt agg gag ctc aac aaa agg aca cag gat ttc tgg gag gtc cag ctc gqc	ELNKRTQDFWEVQLGIPHPAGLKKKKSVTV	gaa ctg aat aag aga acc caa gac ttt tgg gaa gtg caa ctg gga atc cct cac oct got gga ctg aaa aag aaa aag tcc gtq aca dtg	IPHPAGLKKKKSVTVLDVGDAYFSVPLDES	m K~D alt ccc cat ccc gcc ggc ctc aag aaa ag gaa agc gtc acc gtc ctg gat gtg gga gac gct tac ttt agc gtc ccc ctc gac raa $ m xrc$

FIGURE 12 (Cont)

Segment 18			Segment 19		Segment 20		Segment 21		Segment 22
L D V G D A Y F S V P L D E S F R K Y T A F T I P S I N N E K D	Cto gae gto ggo gat gco tat tto too gtg cot otg gat raa rro tto aga aag tat aco got tto aca ato oof and and and	FRKYTAFTIPSINNETPGIRYOYNU1, POGW	Litt agg aam tac aca gcc ttt acc att ccc tcc ayc aat aac gaa acc cct ggc att agg tat cag tat aac gtc rir an one	TPGIRYQYNVLPQGWKGSPAIFOSSMTV1	aca ccc gga atc aga tac caa tac aat gtg ctc ccc caa ggc tgg aag gga tcc ccc scc att ttc caa acc book by	KGSPAIFOSSMTKILEPFRIKNPFM 17 + 12 C C C C C C C C C C C C C C C C C C	K . At tit cag icc age aig mea mag ait eig gag cei itt agg awa	EPFRIKNPEMVIYQYMDDLYVGSDLEIGOG tat	I mag aat occ gaw atg gtg att tac caa tac atg gac gat ctg tat gtg gga agc gat ctg gaa atc gga cas

FIGURE 12 (Cont)

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Segment 26 ccc ttt ctg cat ccc gat agg tgg acc gtc cag cct gac att cag gaw ago tgg aco gto aac gat ato caa aag oto gtg gga aag oto aac tgg goo too cag att tac aco gga ara tgg gga Д Ö П Ø Ö Ø **ፈ** ቤ 3 压 **H** . > 民政 ⋈ Д Д gat tgg aca gtg aat H Z Н ႕ Д gag > O 口 闰 aag cat cag aaa 二 × ĸ ₽ Ŋ 899 8ma Z A E O O Ω Z, gas tcc 出 Д ഗ Z DZ, ctc × 口田 耳 Z Ы ctg aag gag 888 Ы × ¥ Ы 团 gaa gga tac gaa 闰 闰 × Д 闰 asa atc acc cct Д Ö Д × Н > × O Ы H caa cac agg rec cet tte ete tgg atg gge tte aca ccc atc swg Σ © < ₪ HA Н Н 3 K 跘 ĪΨ Н Д 二 O Д Ø CAA cat ctg ctc ara tgg O O ≊ [ī, Н 386 tgg aca gtg > 民民 Д Ö Д gac ctc gag att gaa ccc Н Ы Д Z Н Ы 闰 3 > 闰 Caa aag gac aga 出 X 民 H Ы A E O E Д O Ω '≥ CAC tac gtc ggc tcc gg ctg aga ഗ  $\alpha$ 耳 Д ഗ 999 CBC 口田 Ы ¥ 耳 Ö aag ctc 888 gaa K × 回 Ы > gat 989 989 闰 Д 闰 闰 × tat gac ctc ü Ы Н Д ≯ Д 80 **38**0 × Ы Ω H Ŋ gat rca acc B > O H Σ П att Σ ĸ [I, Z H

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Segment 40	Segment 41	Segment 42	Segment 43	Segment 44	Segment 45
Y V T D R G R Q K V I S I V		O D S G S E V N I V T D  g caa gac tcc ggc tya gag gtc aac att gtg aca gac	ALGIIQAQPDRS L K	VVSQIIEEELIKK L N K Q Q	Y L S W V P A H K G I G A
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Segment 46	Segment 47	Segment 48	Segment 49		Segment 50	
PAHKGIGGNEQVDKLVISGIRK Segment 46 Squent 46 CC gct cat aaa ggc att ggc gga aac gaa cag gtc gac aaa ctg gtc akc kct ggc att agg aaa	VISGIRKVLFLDGINKAQEEHE Segment 47 SA gtg akt kee gga ate aga aag gtg ete ete ete ega ega ate rat aag get eag gaa gag eae gaa	KAQEEHERYHSNWRTMASDFNL Segment48 K aaa gcc caa gag gaa cat gag act act gg agg aca atg gct arc gam ttc aat ctg	MASDFNLPPIVAKEIVANCDKC Segment 49 NE	atg gcc art gas ttt aac ctc ccc cct atc gtc sct aag gaa atc gtc gcc wrt tgc gat aag tgt	VANCDKCQLKGEAMHGQVDCSP Segment 50 S I N	gtg got wro tgt gac aaa tgc cag otc aag gga gag gct atk cac gga cag gto rac tgt agc cot
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FIGURE 12 (Cont)

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Segment 51	Segment 52	Segment 53	Segment 54	Segment 55	Segment 56
QLKGEAMHGQVDCSPGIWQLDCTHLEGKVI . I 	GIWQLDCTHLEGKVILVAVHVASGYIE BAEV  I  1998 atc 199 cag ctc gac 191 acc cat ctg gaa 990 aaa itc att ctg qtc gcc qtc cac gtc gcc tcc gcc tac att gan gct acc	VAVHVAS GYIEAEVIPAETGQ ETAYFILK 1. I. I. Step get geg get age gga tat ate gaa gee gaa gee gaa ace gaa ace gaa ace get tae tte mte ete aag	AETGQETAYFLLKLAGRWPVKVIHTDNG I get gag aca ggc caa gag aca gcc tat tte mtt ctg aaa ctg get gge aga tgg eet gtg ara ryc att cae aca gae aat gge	LAGRWPVKVIHTDNGSNFTSAAVKAACWWA stree good on the grant of the standard of the	

FIGURE 12 (Cont)

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Segment 63		Segment 64	Segment 65		Segment 66		
IWKGPAKLLWKGEGAVVIQD S L	c mtt tgg aaa ggc cct gcc aaa ctg ctc tgg aaa ggc gaa ggc gct gtg gtc atc caa gac	VVIQDNSDIKVVPRRKAKII c gtc gtg att cag gat aac tcc gac att aag gtc gtg cct agg aga aag gct aag att atc	KAKIIRDYGKQMAGDDCVAG S	aga agg asa gcc asa atc att agg gat tac gga aag caa atg gct ggc gmt gac tgt gtg gct rgc	03		
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VIF OVERLAPPING SEGMENTS

FIGURE 12 (Cont)

Segment 6	Segment 7		Segment 8		Segment 9	Segment 10	
EKDWQLGHGVSIEWRQKRYSTQVDPDLADQ R Lyg caw ctg gga cas gga gtg tcc atc gaa tgg aga mag ata agc aca cag gtc gac cct grc ctc gcc gat cas	QKRYSTQVDPDLADQLIHL©YFDCFSDSTI L S G H H H K	mwg aag agm tac tcc acc caa gig gat ccc gri cig gci gac caw cig att cac cic yas tat tic gat igc tit kcc gat agc rca atc	LIHLQYFDCFSDSTIRRAILGQIVRRRCEY H A A HR S Y	ctc atc cat ctg yaw tac ttt gac tgt ttc kct gac tcc rcc att agg aga gcc att ctg gga cas aka gtg agm agg aga tgc gaa tac	RRAILGQIVRRRCEYPSGHNKVGSLQYLALL AL A LHR R S QA agg got atc ctc ggc caw aka gtc agg tgt gag tat cmg kcc gga cac aat aag gtc ggc tcc ctg caa tac ctc gcc ctc		cma ket gge cat aae aaa gtg gga age ete cag tat etg get etg amg get etg att amg eet aag aaa ate ara eec eet etg eet age

FIGURE 12 (Cont)

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Segment 11		Segment 12		
N K P Q K I E H	arg cet ece ete ece tee gtg aaa aag ete ace gaa gae ara teg aat rag eet eaa aag aya	HHWWGH		raa ccc cag aaa ayc aag gga crc aga gra aat cac aca atg aat ggc cat
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VPR OVERLAPPING SEGMENTS

Segment 1		7 Junuangac	Segment 3		Segment 4	
GPQREPYNEWALELLEELKQEA SS	is rgc yct cag aga gag cet tac aat gag tgg rcc etc gag etc etg gaa gag etc aag mam gag get in $\mathbb{R}$	H H C S W H H C W H H C W H H C W H H C W H W H	LHNLGQYIYETYGDTWSGVEAL G H E	tgg ctc cac rrc ctg gga cag yac atc tat gag aca tac gga gac aca tgg kmg gga gtg gaa gcc ctc	WSGVEALIRTLQQLMFIHFRIG E L V	att tac gaa acc tat ggc gat acc tgg kma ggc gtc gag gct ctg atc aga ave ctc cag caa etg mtg tit ric cat tir ara att gga
O	U	60	*	ct tgg	H	at acc
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Σ	arg.		>	gtc	Н	<b>8</b>

FIGURE 12 (Cont)

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Segment 5		Segment 6	
HFRIGCQHSRIGILRQRRAR R I G	rtt cac ttt agg att ggc tgc crg cac tcc agg att ggc att myc aga cag aga agg gsc aga	·	
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H H H	tt myc		
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TAT OVERLAPPING SEGMENTS

# 41/216

Segment 6

FIGURE 12 (Cont)

QTRGGNPTDPKESKKEVASKTETDPCDPCDPDTR BPCDPCDPDPCDP BPCDPPCDPPCAA BPDPCDPCAA BPDPCDPCAA BPDPCDPPCAA BPDPCDPPCAA BPDPCDPPCAA BPDPCDPPPCAA BPDPCAA BPDPCAA BPDPCDPPCAA BPDPCAA BPDP

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Segment 1	Segment 2	Segment 3	Segment 4	Segment 5
GSTDEELLRAVRIINILYQSNPYPS D K I K I K I K 1998 INC 308 986 Ctc Ctd and gct rtc aga atc att as att ctd in the contract of the c	ILYQSNPYPSSEGTRQTRKNRRRW  Atc ctc tac caa agc aat ccc tat ccc wca agc gaa ggc wcc agg caa rcc aga art agg aga agg aga tgg	OTRKNRRRWRARQROIRAISERIL A R cag rct agg ara aac aga agg agg tgg agg cga agg caa atc crc kcc atc tcc gag wgg att ctg	QIRAISERILSTCLGRSAEPVPLQL HS W NF P	RSAEPVPLQLPPLERLHLDCSEDCG P agg yet gec gaa cec gte cec ete cag ete ece eet etg gaa agg ete mac ete gae tgt age gaa gae wgt gre
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REV OVERLAPPING SEGMENTS

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FIGURE 12 (Cont)

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Segment 6		Segment 7	•		Segment 8	
RLHLDCSEDCGTSGTQQSQGTETGVG Segment 6	LV Ctg mac ctg gat tgc tcc gag gat	QQSQGTETGVGRPQISGESSVILGPG Segment 7	A V S	acc caa cag toc cag gga acc gaa acc ggc gtc ggc mrc oct cag att tyg gga gag toc agc gyt rtc etc ggc yec gga	PQISGESSVILGPGTKN  L) AV S  AV S	cc caa atc tya ggc gaa agc tcc gyc rtt ctg gga yct ggc acc aaa aac
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FIGURE 12 (Cont)

VPU OVERLAPPING SEGMENTS

FIGURE 12 (Cont)

ENV OVERLAPPING SEGMENTS

# 46/216

Segment 7		Segment 8		Segment 9
NNMVEQMQEDVISLWDQSLKPCVK Segm D D H I	aat rac atg gtg gam cag atg cam gaa gac xtt atc tcc ctg tgg gac caa agc ctc aag cct tgc gtc aag	D Q S L K P C V K L T P L C V T L N C T N A N L Segm	tgg gat cag tee etg aaa eee tgt gtg aaa etg aca eee ete tge gte ace ete aac tgt ace aat gee aat etg	CHART TO A N L I N V N
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GAP IN SEGMENTS DUE TO HYPERVARIABLE REGIONS 1 AND 2

# 48/216

Segment 1	Segment 2		Segment 3		Segment 4		Segment 5	<b>.</b>
YRLINCNTSVIKQACPKVSFDPIPIHYCTJP SAT tac aga ctg att arc tgt aac aca age gyt atc ama cag gct tgc cct aag rtt ase ttt gas cct atc cct atc cat tac tgt rec cct	PKVSFDPIPIHYC <u>T</u> PAGYAILKCNDKNFNG IT E A F F	ccc asa rtc wcc ttc gam ccc att ccc att cac tat tgc rct ccc gcc gga twc gct atc ctc aag tgt aac rat aag amm ttc aat ggc	AGYAILKCNDKNFNGTGPCKNVSSVQCTHG R K T T T T	A get gge twt gee att etg aaa tge aat rac aaa ama ttt aae gga ace gga eee tgt amg aat gtg tee ase gte eag tgt ace eat gge	TGPCKNVSSVQCTHGIKPVVSTQLLNGSL	c gtg caa tgc aca cac gga atc	IKPVVSTQLLLNGSLAEEIIIRSENLTNN R	att arg cet gig gic age aca cag etc etg etc aac gga age etc gec gaa gag gaa rte rit ate aga age gaa aac ytt ace rat aac

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Segment 6			Segment 7
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		att	
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<u> </u>		gtc	
ENLTNNAKTIIVHLNESVEIN		agc	
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GAP IN SEGMENTS DUE TO HYPERVARIABLE REGIONS 3,4 AND 5

# 50/216

	51/216										
Segment 7		Segment 8		Segment 9	7	Segment 10		Segment 11		Segment 12	1
I E A Q Q H L L Q L T V W G I K Q L Q A R V L A V E R Y	att gag get cag caa cac	ERYLKDOK	asa cag ete cag get agg gee etg get mte gaa agg tat etg asa gae caa mag ytt etg gga mte tgg gge tgt age gga aag	ICTI	gat cag maa ytc ctc ggc mtt tgg gga tgc tcc ggc aaa mtc att tgc aca acc xmt gtg cct tgg aac agc		tgt acc aca mmc gtc ccc tgg aat tcc asc tgg agc aat aag tcc ytc gaa gag att tgg	H O	Yet gag gaa atc tgg rac aat atg aca tgg atk aag tgg gag aga gag att agc aat tac aca arc cwa a	⊁ H	K $D$ $K$ $D$ gas atc toc asc tat acc are the second of
<b>K</b>	gcc	н	atc	×	989	н	atc	ß	<b>a</b> 9c	24	<b>950</b>
R	898	O	<b>3</b> 88	ч	ato	нЪ	att	×	888	闭	Q 6

FIGURE 12 (Cont)

Segment 13	Segment 14	Segment 15	Segment 16	Segment 17	Segment 18
KNEQELLLEIDKWASLNWWFDIT XDA aga aac gaa mag gam ctg ctc gac aaa tgg gct agc ctc tgg aat tgg ttt rac att asc	W N W F D I T N W L W Y I K I F I M I V G G  N S K  tgg aac tgg ttc rat atc wcc aa8 tgg ctg tgg tac att aag att ttc att atg att gtg gga ggc	FIMIVGGLIGGLRIVFAVLSIVN N V I I I I I I I I I I I I I I I I	AVLSIVNRVRQGYSPLSFQTLL T I gct gtg etc agc att rtc aat agg gtc agg caa ggc tat agc cct etg tcc ttc caa acc etc myc	LSFOTLLPAPRGPDRPEGIEEE T ctc agc ttt cag aca ctg myg ccc gct ccc aga ggc cct gac aga cyc gra agc att gag gaa gag	PEGIEEEGGEQDRDRSVRLVSG LGR cyg grag rya atc gaa gag gaa gag gag grc aga agc gtc agg ctc gtg art ggc
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Segment 25		Segment 26		
IEVAQRAGRAILHIPRRIRO V W N T	rtc att gag gtc gyc caa agg gct kgg aga gcc att ctg mat atc cct asa aga atc aga cag			
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>	gtc	R A G R	z	kgg
A	gcc	Ø		960
I A V A E G T D R V G W	att goc gto goc gra kgg aca gac aga	24		aga gcc kgg agg gct atc ctc mac att

NEF OVERLAPPING SEGMENTS

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Segment 1	Segment 2	Segment 3	Segment 4	Segment 5	Segment 6
KWSKSSLVGWPEVRERIRQTPPAAEGV Segme C DA BEGV Segme RAA RAA ata tgg tcc aag wgc tcc cyc gtc gga tgg ccc gma gtg aga gag aga atc aga crg rca scc cct gcc gct gag gga gtg	RIROTPPAAEGVGAVSQDLDKHGAITS Segme RAA *99 att a99 crarcc sct ccc gct gcc gaa ggc gtc ggc gct gyc tcc crg gat ctg gat aag kac gga gcc mtc acc tcc	SODLDKHGAITSSNTPANNADCVWLKA Segmu R Y L A E ago cra gac ctc gac asa kat ggc gct mtt aca ago tcc aat acc act gcc aat aac sct gac tgt gyc tgg ctc rag gct	PANNADCVWLKAQEEEGVGFPVRPQVPSem A PAE acc get aac aat sec gat tgc gyg tgg etg raa gec cag gaa gag gaa gra gtg gga ttt eet gtg aga eec eaa gtg eet	EGVGFPVRPQVPLRPMTYKGAFDLSFF Segmi B gag grg gtc ggc ttc ccc gtc agg cct cag gtc ccc ctg aga cct atg acc tac aaa gea gcc rtc gat ctg tcc ytc ttc	M T Y K G A F D L S F F L K E K G G L E G L V Y S K K Segma A V L L L A B B B B B B B B B B B B B B B B
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Segment 7	Segment 8	Segment 9	Segment 10	Segment 11
LKEKGGLEGLVYSKKRQEILDNWVYHTQGF D I Q D ctc aag gaa aag gga ggc ctc gaa gga ctg rtt tac tcc maa aag agg caa gaa att ctg gat ctg tgg gtg tat mac aca cag gga twc	ROEILDDWWYHTOGFFPDWHNYTPGIRY  N Y Q Y T P G P G I R Y T Q G F F P D W H N Y T P G P G I R Y T P P G P G I R Y T P P G P G I R Y T P P G P G I R Y T P P G P G I R Y T P P G P G I R Y T P P G P P P P P P P P P P P P P P P P	FPDWHNYTPGPGIRYPLTFGWCFKLVPVDPUDPUDPULTFGWCFKLVPVDPUDPULT CCC gat tgg caw aac tat acc cct ggc cct ggc rya agg tat ccc ctc acc ttt ggc tgg tgg caw aac tat acc cct ggc cct ggc rya agg tat ccc ctc acc ttt ggc tgg tgg ttt aag ctc gtg gat ccc	PLTFGWCFKLVPVDPREVEEINKGENNCLLL SAE	REVEEINKGENNCLLHPMSQHGMEDEEREV S A E I NKGENNCLLHPMSQHGMEDEEREV 89w gag gtc gag gaa ryc aat rag gga gag aat aac tgt ctg ctc cac cct ats rgt cwg cat ggc atg gaa gac gaa gas aga gag gtc

FIGURE 12 (Cont)

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Segment 12		Segment 13
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А	gat	闰
EVLIWKF K	a tt	Д
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3	a tg	H
HЖ	80 DD	저 교
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>	a g Ç	Ø
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Radio   Radi	U	Code-	The Genetic Code- First and Second	and		at P	Most Prequently Used Codons	Used	Codons										
MOST Frequently Used Degenerate Codons For TWO or More Amino Acids  T DN RAC/RAT CW TGS/TGK QR CRG/CRA ED GAS/GAM GW KGG/ TT DB GAS/GAM CG KGC/KGT QF SAG/SAA EQ SAG/SAA GD GRC/GRT HD SAC/SAT IN DG GRC/GRT CF TKC/TKT QL CWG/CWA EA GRG/GRA GB GRG/GRA HR CRC/KRT IN DH SAC/SAT CS WGC/WGT QK MAG/WAA EX RAG/RAA GA GSC/RGA HP CWC/CWT IL DW SAC/SAT CY TRC/TKT QP CWG/CWA EV GWG/GWA GA GSC/RGA HP CWC/CWT IL CWC/CWT IT DY KAC/KAT CY TRC/TRT QP CWG/CWA EV GWG/GWA GA GSC/RGA HP CWC/CWT IS TT DV GWC/GWT CY TRC/TRT QP CWG/CWA EV GWG/GWA GA GSC/RGA HP CWC/CWT IS TO GWC/GWT CY TRC/TRT QP CWG/CWA EV GWG/GWA GA GSC/RGA HY YAC/YAT IT TO GWC/GWT CY TRC/TRT QP CWG/CWA EV GWG/GWC LY TAC/YAT IT TO GWC/GWT CY TRC/TRT QP CWG/CWA EV GWG/GWC LY TAC/YAT IT CY CWC/CWT LY TAC/YAT IT CY CWC/CWT CY TRC/TRT GA GRG/GRC LY TAC/YAT IT CY CWC/CWT CY TRC/TRT GA GRG/GRC LY TAC/YAT IT CY CWC/CWT CY TRC/TRT GA GRG/GRC LY TAC/YAT IT CY CWC/CWT CY TRC/TRT GA GRG/GRC LY TAC/YAT IT CY CWC/CWT CY TRC/TRT GA GRG/GRC LY TAC/YAT IT CY CWC/CWT CY TRC/TRT GA GRG/GRC LY TAC/YAT IT CY CWC/CWT CY TRC/TRT GA GRG/GRC LY TAC/YAT IT CY CWC/CWT CY TRC/TRT GA GRG/GRC LY TAC/YAT IT CY CWG/CWT CY TRC/TRT GA GRG/GRC LY TAC/YAT IT CY CWG/CWT CY TRC/TRT GA GRG/GRC LY TAC/YAT IT CY CWG/CWT CY TRC/TRT GA GRG/GRC LY TAC/YAT IT CY CWG/CWT CY TRC/TRC/TRT GA GRG/GRC LY TAC/YAT IT CY CWG/CWT CY TRC/TRC/TRT GA GRG/GRC LY TAC/YAT IT CY CWG/CWT CY TRC/TRC/TRC/TRC/TRC/TRC/TRC/TRC/TRC/TRC/		R Arg		ABD	AAC/AAT	D A SE		, g	rgc/rgr	og u g	CAG/CRA	g]n	GAA/GAG	grà	sac/aan			I Ile 1	ATC/ATT
AC/RAT DN RAC/RAT CW TG8/TGK QR CRG/CRA ED GAS/GAM GW KGG/ HN MAC/MAT IM WC/MAT DR GNC/GMT CR VGC/YGT QE SAG/SAA EQ SAG/SAA GD GRC/GRT HD SAC/SAT IN CAM/CAW TG KGC/KGT HQ CAM/CAW IF AS/AM DG GRC/GRT CF TKC/TKT QL CWG/CWA EA GRG/GRA GB GRG/GRA HR CRC/CKT IR RC/ART DH SAC/SAT CS WGC/WGT QK MAG/WAA EV GWG/GWA GR SGC/RGA HP CWC/CWT IL MC/ANT DY KAC/KAT CY TRC/TRT QP CMG/CWA EV GWG/GWA GR SGC/RGA HP CMC/CWT IS AC/WAT DV GWC/GWT CY TRC/TRT QP CMG/CMA EV GWG/GWA GR SGC/RGT HY YAC/YAT IT IN COMMAN TO WC/CWT I	•	Code-	First	and		Bt F	requently	Used	1 Degene	rate	Codons		TWO OF 1	fore	Amino A	cids			
NEW		IS &	NGLE PO	BITI	NC														
WOG/VGG         NH         MAC/NAT         DA         GMC/GMT         CR         VGC/XGT         QE         SAG/SAA         EQ         SAG/SAT         IN         SAC/SAT         HD         SAG/NGT         HD         CAM/CAM         GE         NGC/NGT         QE         NGC/NGT         QE         NGC/NGT         QE         NGC/NGT         QE         NGC/NGT         QE         NGC/NGT         QE         NGC/NGT         NG         NGC/NGT         QE         NGC/NGT         NG         NGC/NGT         QE         NGC/NGT         NG         NG         NG         NGC		\$	AKT/		RAC/RAT	ä	RAC/RAT		TG8/TGK		CRG/CRA		GAS/GAM		KGG/		MAC/MAT		ATS/ATK
YGC/YGT         NI         AWC/AWT         DB         GAB/GAM         CG         KGC/KGT         QH         CAM/CAW         EA         GMG/GRA         GC         KGC/KGT         HQ         CAM/CAW         EA         GMG/GRA         GC         KGC/KGT         R         CMG/CWA         EA         GMG/GRA         GC         CKC/CKT         IR           CRC/CKT         NS         ARC/ART         CY         TRC/TKT         QL         CWG/GWA         EX         GRG/GRA         GR         GRG/GRA         HL         CWC/CWT         IL           ARA         NY         WAC/WAT         DY         CMC/GWT         CY         TRC/TRT         QP         CWG/CWA         EV         GWG/GWA         HP         CMC/CWT         IS           CSC/CST         NY         WAC/WAT         DV         CMC/GWT         CY         TRC/TRT         QP         CWG/GWC         RC         GC         CMC/CWT         IS           CSC/CST         CKG/CKC         CKG/CKC         CKG/CKC         CKG/CKC         CKG/CKC         IC         CKG/CKC         IC		2	WOG/YGG		MAC/NAT	á	GMC/GMT		YGC/YGT		SAG/SAA		SAG/SAA		GRC/GRT		SAC/SAT		AWC/AWT
CRG/CRA         NK         AAS/AAM         DG         GRC/GRT         CF         TKC/TKT         QL         CWG/CWA         EG         GRG/GRA         GE         GRG/GRA         HR         CRC/CRT         IL           ARG/ARA         NT         ANC/ANT         DY         XAC/KAT         CY         TRC/TRT         QP         CMG/CWA         EV         GWG/GWT         HP         CWC/CWT         IL           ALA         NY         WAC/WAT         DV         QWC/GWT         CY         TRC/TRT         QP         CMG/CWA         EV         GWG/CWT         HP         CWC/CWT         IL           BGC/RGA         NY         WAC/WAT         DV         QWC/CWT         TR         TT         TT <td></td> <td><b>2</b></td> <td>YGC/YGT</td> <td></td> <td>AWC/AWT</td> <td>S</td> <td>GAS/GAM</td> <td></td> <td>KGC/KGT</td> <td></td> <td>CAM/CAW</td> <td></td> <td>GMG/GMA</td> <td></td> <td>KGC/KGT</td> <td></td> <td>CAM/CAW</td> <td></td> <td>WTC/WTT</td>		<b>2</b>	YGC/YGT		AWC/AWT	S	GAS/GAM		KGC/KGT		CAM/CAW		GMG/GMA		KGC/KGT		CAM/CAW		WTC/WTT
CRC/CRT N6 ARC/ART DH SAC/SAT CS WGC/WJT QK MAG/MAA EK RAG/RAA GA GSC/GST HL CWC/CWT IL ARG/ARA NT ANC/ART DY YAC/YAT CY TRC/TRT QP CMG/CMA EV GWG/GWA GR SGC/RGA HP CMC/CMT IS AKA) AKA AKA SGC/RGA CSC/CST GV GKG/GKC TXC/YAT IT GS CKG/GKC TXC/YAT IT TX CSC/CST TX ASA/ASG CKG/GKC TXC/WGT		8	CRG/CRA		AAS/AAM	8	GRC/GRT		TKC/TKT		CWG/CWA		GRG/GRA		GRG/GRA		CRC/CRT		AKA/
ARG/ARA NT AMC/ANT DY KAC/KAT CY TRC/TRT QP CMG/CMA EV GWG/GWA GR SGC/ROA HP CMC/CMT IS ALGA.  BACA/ROA NY WAC/WAT DV GWC/GWT CY TRC/TRT QP CMG/CMA EV GWG/GWA GR GCC/ROT HY YAC/YAT IT SCC/ROA CSC/CST  BACA/ROA  BASA/ASG  CKC/CCC  CKC/MCT  MCC/MCT		*	CRC/CRT		ARC/ART	ä	SAC/SAT		WGC/WGT		MAG/MAA		RAG/RAA		GSC/GST		CWC/CWT		MTC/MTT
AKA/ NY WAC/WAT DV GWC/GWT GS RGC/RGT HY YAC/YAT IT SGC/RGA SGC/RGT HY YAC/YAT IT CSC/CST CSC/CST A8A/A3G CKG/CKC CKG/CKC MGC/MGT		ž	ARG/ARA		AMC/ANT	ă	XAC/XAT		TRC/TRT		CMG/CMA		GWG/GWA		SGC/RGA		CMC/CMT		AKC/AKT
9GC/RGA CSC/CST A8A/A3G CKC/CCC CKC/CCC CKC/CCC CKC/MGT		R.	ACA/		WAC/WAT	2	GWC/GWT								RGC/RGT		YAC/YAT		AYC/AYT
CSC/CST IN ABA/ASG IN CKC CKC MGC/MGT		2	SGC/RGA												GKG/GKC				RTC/RTT
		80	CSC/CST																AWA/
		R.	ASA/ASG																
		3	CKG/CKC																
		88	MGC/MGT																

FIGURE

Single letter code

X = C or T

X = G or T

S = C or G

W = A or T

H = A or C or T

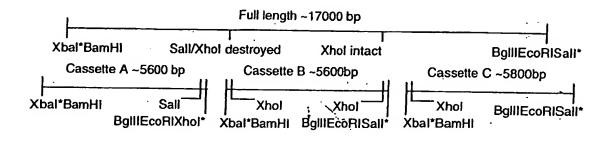
U = A or C or T

N = A or C or T

A STEEL BOOK STATE

	CTG/CTC			MYG/WTG TKG/	TYG/TYA CWG/CWA	CWC/CWT	YTC/YTT MTC/MTT	CYC/CYG STG/STC CKG/CKC	59/216	
	r Leu			53:	32	<b>'</b> :	ΞÉ	និនិនិ		
	GTG/GTC			RTG/ GWC/GWT	KTC/KTT	RTC/RTT	GKG/GKC	STG/STC		
	v Val	Acids		<b>\$</b> 9	2 A	1 5	\$ 8	Ŗ		
	y Tyr TAC/TAT	More Amino Acids		WAC/WAT KAC/KAT	YAC/YAT	TWC/TWT	*** / - W *			
	¥	More		<b>\$9</b> \$	<b>4</b> E	¥ ×	•			
	TGG/	TWO or		WGG/YGG KGG/ TEG/	TKG/	TGS/TGK				
	a ti	For		# 5 %	3 3	ပ္				
	T Thr ACC/ACA	e Codone		AYG/ AMC/AMT	AYC/AYT	ASA/ASG	ASC/WCC			
811	Tabr	nerat		£25	;	e e	18			
Frequently Used Codons	AGC/TCC	Frequently Used Degenerate Codons		TSG/ ARC/ART TYG/TYA	WGC/WGT	TYC/TYT TMC/TMT	AKC/AKT	RGC/RGT YCC/YCT ASC/WCC		
tly u	Ser	tly u		SSS	2	8 X	18	8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8		•
Frequen	כככ/ככב	Frequen		CMG/CMA CMC/CMT 8CC/SCT	CSC/CST	YCC/YCT	MCC/MCT			
Most	P to	Most		252	<b>%</b> ;	3 8	ž.			
Second	דדכ/דדד	Second	NO	TKC/TKT WTC/WTT YTC/YTT	TYC/TYT	KTC/KTT				
and	P Phe	and	SITI	212	82	: 2				
- Pirst	ATG/	- First	AT A SINGLE POSITION	AKT/ ATS/ATK MTG/WTG	AWG/	RTG/				or T
Code	A B	Code	RAI	ăzz	ž į	<b>£</b>			# 0000 #####	ซ ห
The Genetic Code- Pirst and Second Most	AAG/AAA	Genetic Code- First and Second Most	BASES	AWG/ AAB/AAM MAG/MAA	RAG/RAA	AMA/DMA	AWA		# 0 6 6 0 6 0 0 0 0	א סול כ
The	Ľy8	The	TWO	<b>5</b> 88	Ð 6	į	Ħ		C C E E E E E E E E E E E E E E E E E E	0 Z

FIGURE 13 (cont)



Full length construction after cloning the cassettes into pBS Sites marked with a \*\*\* are in the pBS MCS

# Cassette Extras (Can be removed from cassette ends)

5' gc ggatccacc atggtcgac tga agatct gaattc gc 3' B (43bp) BamHl/Kozak Start Xhol Xhol Stop Bglil EcoRl
The state of the s
5' gc ggatccacc atg ctcgagctcgag tga agatgt gaattc gc 3' C (37bp) BamHI/Kozak Start Xhol Stop Bgill EcoRI
5' gc ggatccacc atg ctcgagtga agatct gaattc qc 3'

# FIGURE 14

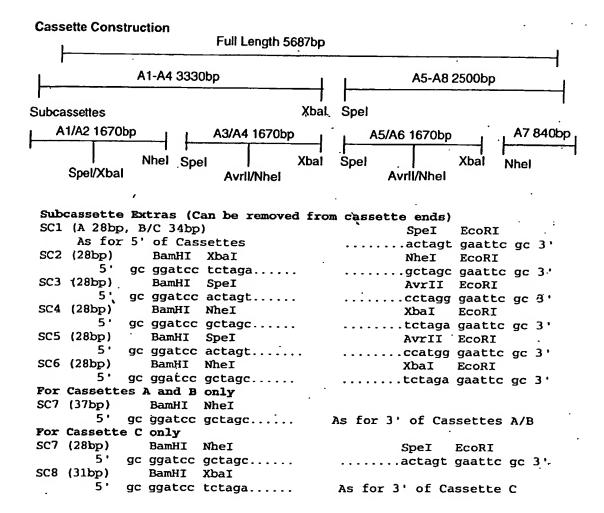


FIGURE 14 (Cont)

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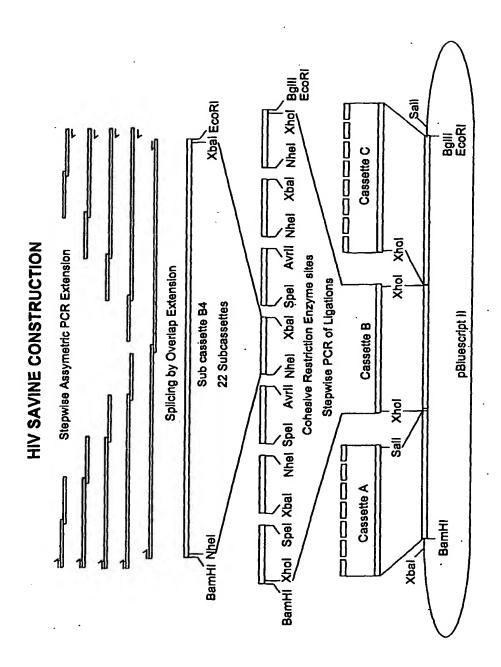


FIGURE 14 (Cont)

WO 01/090197 PCT/AU01/00622

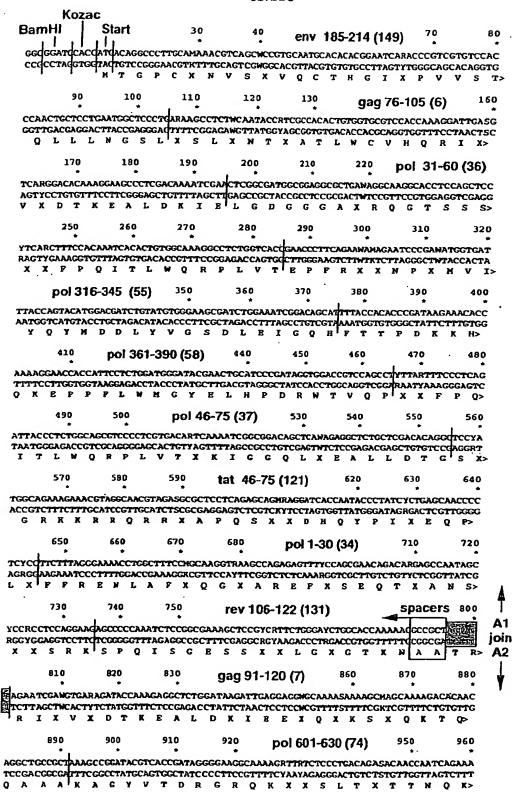


FIGURE 15

WO 01/090197 PCT/AU01/00622

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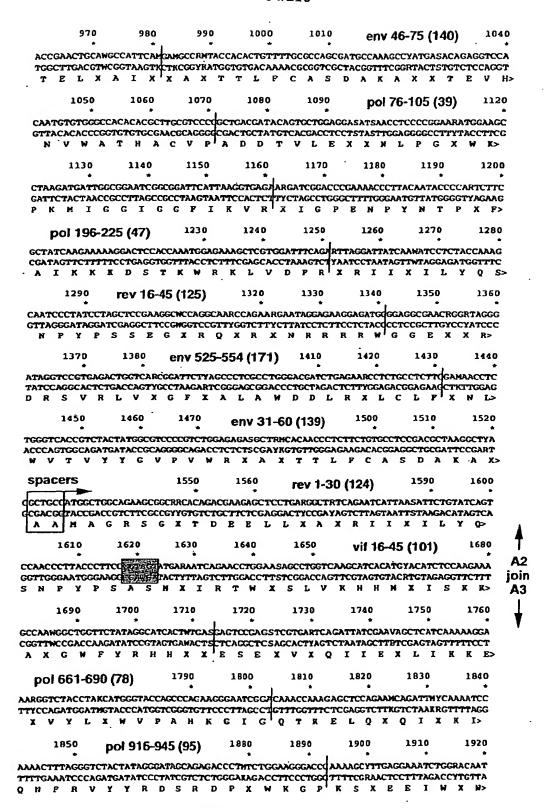


FIGURE 15 (Cont)
SUBSTITUTE SHEET (RULE 26)

1930							
	env 40	5-434 (163)	1960	1970	1980	1990	2000
ATGACATGGAT	KSAGTGGGAG.	AGAGAGATTAGC	* AATTACACA	* ARCCWAATCTA	* TRAGATTCTY	ARACCCGA	ACCCACAGC
TACTGTACCTA	MSTCACCCTC	TCTCTCTAATCG	TTAATGTGT	TYGGETTAGAT	AVTTABLE	TVTCCCCT	Necemente
M T W X	X M P	REIS	N Y T	YYTV	XIL		PTA
.,				A A 1 1	X 1 D	A P E	PTA
2010	2020	gag 451-	480 (31)	2050	2060	2070	2080
CCCTCCCGCTG	AGARTTTCRGA	TTCGCTGAGGA	ACTACACC	CTCCCHAAAGC	NAGAGCHAAA	GGATAAGGA	dCAATACG
		PAAGCCACTCCT					
PPAI	XPX	PGEE	ттр	S X K (	e x x	D K E	Q Y>
2000	2100	77.50					
2090	2100	2110	poi 108	5-135 (41)	2140	2150	2160
ATCAGATTHTTA	TTGAGATTTG	CCCCAAGAAACC	TATTGGTAG	CACTECTCCTCC	CACCTACCC	CTYCTICA ATTA	TC ATTCCC
TAGTCTAAKAAT							
		G K K A					I I G>
_							
2170	2180	2190	2200	vpr 46-75	5 (115)	2230	2240
		•		•	• •	•	•
AGPATTTACGAA							
TCTTAAATGCTT							
RII.Y E	TYGI	TWE	GVE	ALIR	X L Q	Q.LX	F X H>
2250	2260	2270	2280	2290	tat 31-6	1 (120)	2320
	L	•	*			•	
TTTCAGAATCGG							
AAAGTCTTAGCCT						CCTTCCTTT	TTCTCTT
FRIG	'с х н	C O X C	F L T	K C T G	I S X	G R K	K R>
2330	2340	spacers		2370	2380 ta	t 1-30 (1	10)
•	• •	<del>·</del>		•	*	•	•
RACAGAGAAGGSG							
YIGICICITCCSC	TCGACCCCTI	CCACCCTACCTC	GGGCACCT(	CCCTTSGACCT	CCCAACCTTI	#GTCGGACC	GACCCTC
XQRRX	A P O	A A M D	PVD	PXLE	'P W X	H P G	S Q>
2410	2420	2430	2440	2450	2460	2470	2480
•	•	•	•		•	•	•
CCTAMGACAGCCT	GTWMCAAATG	TATTGCAAAAA	TGGGGG	GAAGAGACAA	CCCCTAGCCM	GAAACAGGA	ACMGAA A
GGATKCTGTCGGA	CAWKGTTTACC	SATAACGTTTTT	ACCECARE	CTTCTCTGTT	GGGATCGGR	CTTTGTCCT	TGKCTT I
PXTA			CDC			K O F	X K>
	CXKC	YCKK					
	C X K C	YCKK	C F S		PSX		•
gag 466-4		2510	2520 .	2530	2540	2550	2560
gag 466-4	95 (32)	2510	2520 .	2530	2540	2550	•
AGACAAAGAACNC1	95 (32)	2510 * AGCCAGCCTCAA	2520 . GTCCCTGT	2530 TTGCCAATGAGA	2540 • ATTTCAATA	2550 TGTGGAAGA	* ATRACA
AGACAAAGAACWC1 TCTGTTTCTTGWG/	95 (32) РАССССССТТУ РТЕСЕСЕВАЛЯ	2510 * AGCCAGCCTCAA TCGGTCGGAGTT	2520 . * GTCCCTGT CAGGGACA	2530 TTGCCAATGACA AACCGTTACTGT	2540 * ATTTCAATA TAAAGTTAT	2550 TGTGGAAGA	* ATRACA
AGACAAAGAACNC1	95 (32) РАССССССТТУ РТЕСЕСЕВАЛЯ	2510 * AGCCAGCCTCAA	2520 . * GTCCCTGT CAGGGACA	2530 TTGCCAATGACA AACCGTTACTGT	2540 ATTTCAATA TAAAGTTAT	2550 ± TGTGGAAGA ACACCTTCT	* ATRACA
AGACAAAGAACNC1 TCTGTTTCTTGNGA D K E X	95 (32) PACCCCCCTTY PTGGGGGGAAR Y P P X	2510  *AGECAGECTEAN TEGGTEGGAGTT  A S L K	2520 . * GTCCCTGT CAGGGACA	2530 TTGCCAATGACA AACCGTTACTGT	2540 * ATTTCAATA TAAAGTTAT	2550 ± TGTGGAAGA ACACCTTCT	+ ATRACA TAYTGT
AGACAAAGAACNC1 TCTGTTTCTTGNGA D K E X	95 (32) РАССССССТТУ РТЕСЕСЕВАЛЯ	2510  *AGECAGECTEAN TEGGTEGGAGTT  A S L K	2520 . * GTCCCTGT CAGGGACA	2530 TTGCCAATGACA AACCGTTACTGT	2540 * ATTTCAATA TAAAGTTAT	2550 ± TGTGGAAGA ACACCTTCT	+ ATRACA TAYTGT
AGACAAAGAACWCT TCTGTTTCTTGWG/ D K E X 2570 6	95 (32) PACCCCCTTY PTGGGGGGAAR Y P P X PNV 91-120	2510  *AGECAGCCTCAA TCGGTCGGAGTT : A S L K	2520 . GTCCCTGT CAGGGACA S L 1	2530 TTGGCAATGAGA AACCGTTACTGT P G N D	2540  ATTTCAATA  TAAAGTTAT  N F N  2620	2550 TGTGGAAGA ACACCTTCT H W K	ATRACA TAYIGT N X> 2640
AGACAAAGAACNCT TCTGTTTCTTGMG/ D K E X  2570 6	95 (32) PACCECCTTY PTGGGGGGAAR Y P P X PINV 91-120 CAMGAAGACR	2510  AGECAGECTEAN  TEGGTEGGAGTT  A S L K  (143)  TTATETEACTAT	2520 .  GTCCCTGT CAGGGACA  S L 1  2600  GGGACCAA	2530 PTCCCAATGAC AACCGTTACTGT P G N D 2610 AGCCTCAAGCCT	2540 LATITCAATA TAAAGTTAT N P N 2620 TGCGTCAAG	2550 TGTGGAAGA ACACCTTCT H W K  2630 CTCGACGTC	ATRACA TAYTGT N X> 2640 CCCGAT
AGACAAAGAACWCT TCTGTTTCTTGWG/ D K E X 2570 6	95 (32) PACCECCTTY PTGGGGGGAAR Y P P X PINV 91-120 CAMGAAGACR	2510  AGECAGECTEAN  TEGGTEGGAGTT  A S L K  (143)  TTATETEACTAT	2520 .  GTCCCTGT CAGGGACA  S L 1  2600  GGGACCAA	2530 PTCCCAATGAC AACCGTTACTGT P G N D 2610 AGCCTCAAGCCT	2540 LATITCAATA TAAAGTTAT N P N 2620 TGCGTCAAG	2550 TGTGGAAGA ACACCTTCT H W K  2630 CTCGACGTC	ATRACA TAYTGT N X> 2640 CCCGAT
AGACAAAGAACNCT TCTGTTTCTTGNGA D K E X 2570 ( TGGTGGANCAGATG	95 (32) PACCECCTTY PTGGGGGGAAR Y P P X PINV 91-120 CAMGAAGACR GTKCTTCTGY	2510  AGECAGECTEAN  TEGGTEGGAGTT  A S L K  (143)  TTATETEACTAT	2520 . GTCCCTGT CAGGGACA S L 1 2600 GGGACCAAA	2530 PTCCCAATCAC AACCGTTACTCT P G N D  2610 AGCCTCAACCCT	2540 LATITCAATA TAAAGTTAT N P N 2620 TGCGTCAAG	2550 TGTGGAGA ACACCTTCT H W K 2630 CTCGACGTCGAGGTGGAGGTGCAGG	ATRACA TAYTGT N X> 2640 CCCGAT
AGACAAAGAACNCT TCTGTTTCTTGNGA D K E X 2570 ( TGGTGGANCAGATG	95 (32) PACCECCTTY PTGGGGGGAAR Y P P X PINV 91-120 CAMGAAGACR GTKCTTCTGY	2510  AGECAGCCTCAA TCGGTCGGAGTT  A S L K  (143) TTATCTCACTAT AATAGAGTGATA	2520 . GTCCCTGT CAGGGACA S L 1 2600 GGGACCAAA	2530 PTCCCAATCAC AACCGTTACTCT P G N D  2610 AGCCTCAACCCT	2540 LATTICANTA TANAGTTAT N F N 2620 TGCGTCAAG	2550 TGTGGAGA ACACCTTCT H W K 2630 CTCGACGTCGAGGTGGAGGTGCAGG	ATRACA TAYIGT N X>  2640  CCCCAT
AGACAAAGAACNCT TCTGTTTCTTGNGA D K E X 2570 ( TGGTGGANCAGATG	95 (32) PACCCCCCTTY PTGGGGGGAAR Y P P X PINV 91-120 CAMGAAGACR GTKCTTCTGY.	2510  AGECAGCCTCAA TCGGTCGGAGTT  A S L K  (143) TTATCTCACTAT AATAGAGTGATA	2520 GTCCCTGT CAGGGACA S L 1 2600 GGGACCAA CCCTGGTTT N D Q	2530 PTCCCAATGACA AACCGTTACTGT P G N D  2610 AGCCTCAAGCCT CCGGAGTTCGGA S L K P	2540 LATTICANTA TANAGTTAT N F N 2620 TGCGTCAAG	2550 TGTGGAGA ACACCTTCT H W K 2630 CTCGACGTCGAGGTGGAGGTGCAGG	ATRACA TAYIGT N X>  2640  CCCCAT
AGACAAAGAACHCT TCTGTTTCTTGHGA D K E X 2570 C TGGTGGAHCAGATG ACCACCTKGTCTAC I V X Q H 2650	95 (32) PACCECCTTY PTGGGGGGANR Y P P X PINV 91-120 CAMGANGACR GTKCTTCTGY. X B D :	2510  AGCCAGCCTCAA ATCGGTCGGAGTT  A S L K	2520 .  GTCCCTGTT CAGGGACAA  2600 GGGACCAA  CCCTGGTTT N D Q  (51)	2530 TTCCCAATGACA AACCGTTACTGT P G N D  2610 AGCCTCAAGCCT CCGGAGTTCGGA S L K P  2690	2540  AATTTCAATA TAAAGTTAT N F N  2620 TGCGTCAAG ACGCAGTTG C V K	2550 TGTGGAAGA ACACCTTCT H W K  2630 TTCGACGTCC BAGCTGCAGC L D V  2710	ATRACA TAYIGT N X>  2640  CCCCATA C D>  2720
AGACAAAGAACNCT TCTGTTTCTTGNGA D K E X  2570 E TGGTGGAHCAGATG ACCACCTKGTCTAC 4 V X Q M  2650 CCCTATTTCTCCGT	95 (32) PACCECCTTY PTGGGGGGANR Y P P X PINV 91-120 CAMGANGACR GTKCTTCTGY. X E D 3 2660 GCCTCTGGATI	2510  AGECAGECTEAN TEGGTEGGAGTT  A S L K  (143) TTATETEACTAT AATAGAGTGATA X I S L V  pol 256-285	2520 .  GTCCCTGT CAGGGACAA CCCTGGTT N D Q  (51) AAGTATACC	2530 TTCCCAATCACA AACCGTTACTGT P G N D  2610 AGCCTCAAGCCT NCGGAGTTCGGA S L K P  2690	2540 AATTTCAATA TAAAGTTAT N P N 2620 TGCGTCAAG ACGCAGTTC C V K 2700	2550 TGTGGAAGA ACACCTTCT H W K  2630 CTCGACGTCGAGGTGGAGCTGCAGG L D V  2710	ATRACA TAYTGT N X> 2640 GGCGAT CCGCTA G D> 2720
AGACAAAGAACHCT TCTGTTTCTTGHGA D K E X 2570 C TGGTGGAHCAGATG ACCACCTKGTCTAC I V X Q H 2650	95 (32) PACCECCTTY PTGGGGGGANR Y P P X PINV 91-120 CAMGANGACR GTKCTTCTGY. X E D 3 2660 GCCTCTGGATI	2510  AGECAGECTEAN TEGGTEGGAGTT  A S L K  (143) TTATETEACTAT AATAGAGTGATA X I S L V  pol 256-285	2520 .  GTCCCTGT CAGGGACAA CCCTGGTT N D Q  (51) AAGTATACC	2530 TTCCCAATCACA AACCGTTACTGT P G N D  2610 AGCCTCAAGCCT NCGGAGTTCGGA S L K P  2690	2540 AATTTCAATA TAAAGTTAT N P N 2620 TGCGTCAAG ACGCAGTTC C V K 2700	2550 TGTGGAAGA ACACCTTCT H W K  2630 CTCGACGTCGAGGTGGAGCTGCAGG L D V  2710	ATRACA TAYTGT N X> 2640 GGCGAT CCGCTA G D> 2720
AGACAAAGAACNCT TCTGTTTCTTGNGA D K E X  2570 E TGGTGGAHCAGATG ACCACCTKGTCTAC 4 V X Q M  2650 CCCTATTTCTCCGT	95 (32) PACCECCTTY PTGGGGGGAAR Y P P X PINV 91-120 CAMGAAGACR GTKCTTCTGY X B D 3 2660 GCCTCTGGATI	2510  CAGECAGCCTCAA CCGGTCGGAGTT  A S L K  COMMENTAL COM	2520 . GTCCCTGT CAGGGACAA S L 1 2600 GGGACCAAA CCCTGGTTT N D Q (51) AAGTATACC	2530 PTCCCAATCACA AACCGTTACTGT P G N D  2610 AGCCTCAAGCCT ACGGAGTTCGGA S L K P  2690 AGCTTCACAATCCCGAAGTGTTACCGAAGTGTTACCCACAATCCCGAAGTGTTACCCGAAGTCCCAACCCCTCCAACCCAACCCCAACCCAACCCAACCCAACCCAACCCAACCCAACAACCAACCAACCAACCAACAACCAACAACAACCAACCAACCAACCAACCAACCAACCAACCAACCAACAACCAACAACCAACCAACAACAA	2540  AATTCAATA TAAAGTTAT N F N  2620 TGCGTCAAG ACGCAGTTC C V K  2700 CCCTAGCAY/	2550 TGTGGAAGA ACACCTTCT H W K  2630 CTCGACGTCGAGCTGCAGC L D V  2710 AACAATGACTTACTC	ATRACA TAYTGT N X> 2640 GGCGAT CCGCTA G D> 2720 GCAACT GTTGA
AGACAAAGAACNCT TCTGTTTCTTGNG D K E X  2570 6 TGGTGGANCAGATG ACCACCTKGTCTAC V X Q N  2650 CCCTATTTCTCCGT	95 (32) PACCECCTTY PTGGGGGGAAR Y P P X PINV 91-120 CAMGAAGACR GTKCTTCTGY X B D 3 2660 GCCTCTGGATI	2510  CAGECAGCCTCAA CCGGTCGGAGTT  A S L K  COMMENTAL COM	2520 . GTCCCTGT CAGGGACAA S L 1 2600 GGGACCAAA CCCTGGTTT N D Q (51) AAGTATACC	2530 PTCCCAATCACA AACCGTTACTGT P G N D  2610 AGCCTCAAGCCT ACGGAGTTCGGA S L K P  2690 AGCTTCACAATCCCGAAGTGTTACCGAAGTGTTACCCACAATCCCGAAGTGTTACCCGAAGTCCCAACCCCTCCAACCCAACCCCAACCCAACCCAACCCAACCCAACCCAACCCAACAACCAACCAACCAACCAACAACCAACAACAACCAACCAACCAACCAACCAACCAACCAACCAACCAACAACCAACAACCAACCAACAACAA	2540  AATTCAATA TAAAGTTAT N F N  2620 TGCGTCAAG ACGCAGTTC C V K  2700 CCCTAGCAY/	2550 TGTGGAAGA ACACCTTCT H W K  2630 CTCGACGTCGAGCTGCAGC L D V  2710 AACAATGACTTACTC	ATRACA TAYTGT N X> 2640 GGCGAT CCGCTA G D> 2720 GCAACT GTTGA
AGACAAAGAACNCT TCTGTTTCTTGNG D K E X  2570 6 TGGTGGANCAGATG ACCACCTKGTCTAC V X Q N  2650 CCCTATTTCTCCGT	95 (32) PACCECCTTY PTGGGGGGAAR Y P P X PINV 91-120 CAMGAAGACR GTKCTTCTGY X B D 3 2660 GCCTCTGGATI	2510  CAGCCAGCCTCAA  CTCGGTCGGAGTT  A S L K  COMMITTATCTCACTAT  AATAGAGTGATA  X I S L  POI 256-285  RAARRCTTCAGAA  CTTYYGAAGTCTT  X X F R	2520 .  GTCCCTGTT CAGGGACAA  GGGACCAAA  CCCTGGTTT N D Q  (51)  AAGTATACC TCATATGG K Y T	2530 PTCCCAATGADA AACCGTTACTGT P G N D  2610 AGCCTCAAGCCT CGGAGTTCGGA S L K P  2690 AGCTTCACAATCCGAAGTGTTACCGAAGTGTTACAAATCGTATACCCAAAGTGTTACAAATCCGAAAATCCGAAAGTGTTACAAATCCGAAAGTGTTACAAATCCGAAAGTGTTACAAATCCGAAAGTGTTACAAATCCGAAAGTGTTACAAATCCGAAAATCCGAAAGTGTTACAAATCCGAAAATCCGAAAATCCGAAAATCCGAAAATCCGAAAATCCGAAATCCAAATCCGAAAATCCGAAAATCCGAAAATCCAAAATCCAAAATCCAAAATCCAAAATCCAAAATCCAAAATCCAAAATCCAAAATCAAAAATCCAAAAATCCAAAATCCAAAAAA	2540 AATTICANTA TANAGTTAT N P N 2620 TGCGTCAAG ACGCAGTTC C V K 2700 CCCTAGCAYA GGGATCGTRA P S X	2550 TGTGGAAGA ACACCTTCT H W K  2630 CTCGACGTCGAGCTGCAGC L D V  2710 AACAATGACTTACTC	ATRACA TAYTGT N X> 2640 GGCGAT CCGCTA G D> 2720 GCAACT GTTGA
AGACAAAGAACHCT TCTGTTTCTTGHGA D K E X  2570 E TGGTGGAHCAGATG ACCACCTKGTCTAC 1 V X Q M  2650 ECCTATTTCTCCGT TGGATAAAGAGCA A Y P S V  2730	95 (32) PACCECCTTY PTGGGGGGGANR Y P P X PINV 91-120 CAMGANGACR GTKCTTCTGY X B D : 2660 GCCTCTGGATI CGGAGACCTAT P L D 2740	2510  AGECAGCCTCAA ATCGGTCGGAGTT  A S L K  D (143)  TTATCTCACTAT AATAGAGTGATA  X I S L  POI 256-285  RAARRCTTCAGAI  TTYYGAAGTCT  X X P R  2750 PO	2520 .  GTCCCTGTTC CAGGGACAN CCCTGGTTT W D Q  (51) AAGTATACC TCATATGG K Y T	2530 TTCCCAATCACA AACCGTTACTGT P G N D  2610 ACCCTCAACCCT CCGCAGTTCCCAA S L K P  2690 CCTTTCACAAT CCGAAGTGTTAC A P T I  30 (84)	2540  ATTTCAATA TAAAGTTAT N P N  2620 TGCGTCAAG ACGCAGTTG C V K  2700 CCCTAGCAY/ GGGATCGTRY P S X	2550 TGTGGAAGA ACACCTTCT H W K  2630 TCGACGTCGACGTCGACGTGCAGCTGCAGCTGCAGCTGCAGCTGCAGCTGCAGCTGCAGCTGCAGCTGCAGCTGCAGCTGCAGCTGCAGCAATGAAATGAAAATGAAAATGAAAATGAAAATGAAAATGAAAATGAAAATGAAAAATGAAAAAA	ATRACA TAYTGT N X> 2640 CCCCAT CCCCTA G D> 2720 CAACT GTTGA Q L> 2800
AGACAAAGAACNCT TCTGTTTCTTGNGF D K E X  2570 E TGGTGGANCAGATG ACCACCTKGTCTAC 4 V X Q N  2650 CCCTATTTCTCCGTCTGGATAAAGAGGCAA A Y P S V  2730 CAAAGGCGAAGCCAT	95 (32)  PACCECCTTY PTGGGGGGAAR Y P P X  PINV 91-120  CAMGAAGACR GTKCTTCTGY. X R D  2660  SCCTCTGGATT CGGAGACCTAT P L D  2740  PSCATGGCCAA	2510  CAGECAGCCTCAA CTCGGTCGGAGTT  A S L K  C (143)  TTATCTCACTAT AATAGAGTGATA X I S L V  POI 256-285  RAARRCTTCAGAI TTYYGAAGTCTT X X F R  2750 po	2520 .  GTCCCTGTTC CAGGGACAA  CCCTGGTTT N D Q  (51)  AAGTATACC TTCATATGG K Y T  DI 751-78	2530 TTGCCAATGAD ACCGTTACTGT P G N D  2610 AGCCTCAAGCCT NCGGAGTTCGGA S L K P  2690 AGCTTTCACAAT CGAAAGTGTTAC A P T I  30 (84) TTGGCAACTGG	2540  ATTTCAATA TAAAGTTAT N P N  2620 TGCGTCAAGA ACGCAGTTC C V K  2700 CCCTAGCAYA GGGATCGTRT P S X  2780	2550 TGTGGAAGA ACACCTTCT H W K  2630 CTGGACGTCGAGGTGGAGCTGCAGGTGCAGGTGCAGGTGCAGGTGCAGGTGCAGGGGGGGG	ATRACA TAYTGT N X> 2640 CCCCAT CCCCTA G D> 2720 CCAACT GTTGA Q L> 2800
AGACAAAGAACNCT TCTGTTTCTTGNGF D K E X  2570 ( TGGTGGAMCAGATG ACCACCTKGTCTAC Y X Q N  2650 CCCTATTTCTCCGTT TGGATAAAGAGCCAA A Y P S V  2730 CAAAGGCGAAGCCAT TTTCCGCTTCGGTT	95 (32) PACCECCTTY PTGGGGGGAAR Y P P X PINV 91-120 CAMGAAGACR GTKCTTCTGY X E D : 2660 GCCTCTGGATT CGGAGACCTA P L D 2740 PSCATGGCCAA	2510  CAGCCAGCCTCAA TCGGTCGGAGTT  A S L K  O (143)  TTATCTCACTAT AATAGAGTGATA AX I S L V  POI 256-285  RAARRCTTCAGAI TTYYGAAGTCT X X P R  2750 PO AGTGRATTGCTCA CACYTAACGAGT	2520 GTCCCTGTTTCAGGGACAAACCCCCTGGTTTTN D Q (51) AAGTATACCCTCATATGG K Y T COI 751-78	2530 PTCCCAATGACAACCCTTACTGT PGND 2610 AGCCTCAAGCCT AGCGATTCGGA SLKP 2690 AGCTTCACAATCCGAAAGTGTTACAAATCCGAAAGTGTTACAATTCACAATTCACAATTCACAATTCACAATTCACAATTCACAAACCGTTACCCAACCCGAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCTTGACCCTTGACCCAACCCGTTGACCCTTGACCTTGACCTTTGACCTTTGACCTTTACTTTACTTTACTTTACTTTACTTAC	2540  ATTICANTA TANAGTIAT N P N  2620  TECGTCAAG ACGCAGTTC C V K  2700  ECCTAGCAYA EGGATCGTRI P S X  2780  ATTICACACA AACGTGTGT	2550 TGTGGAAGA ACACCTTCT H W K  2630 CTGGACGTC SAGCTGCAG L D V  2710 AACAATGAC TTGTTACTT N N E  2790 CCTGGAGGGGGGACCTCCC	ATRACA TAYTGT N X> 2640 GGCGAT CCGCTA G D> 2720 CAACT GTTGA Q L> 2800 CAAAGR TTTCY
AGACAAAGAACNCT TCTGTTTCTTGNGF D K E X  2570 E TGGTGGANCAGATG ACCACCTKGTCTAC 4 V X Q N  2650 CCCTATTTCTCCGTCTGGATAAAGAGGCAA A Y P S V  2730 CAAAGGCGAAGCCAT	95 (32) PACCECCTTY PTGGGGGGAAR Y P P X PINV 91-120 CAMGAAGACR GTKCTTCTGY X E D : 2660 GCCTCTGGATT CGGAGACCTA P L D 2740 PSCATGGCCAA	2510  CAGCCAGCCTCAA TCGGTCGGAGTT  A S L K  O (143)  TTATCTCACTAT AATAGAGTGATA AX I S L V  POI 256-285  RAARRCTTCAGAI TTYYGAAGTCT X X P R  2750 PO AGTGRATTGCTCA CACYTAACGAGT	2520 GTCCCTGTTTCAGGGACAAACCCCCTGGTTTTN D Q (51) AAGTATACCCTCATATGG K Y T COI 751-78	2530 PTCCCAATGACAACCCTTACTGT PGND 2610 AGCCTCAAGCCT AGCGATTCGGA SLKP 2690 AGCTTCACAATCCGAAAGTGTTACAAATCCGAAAGTGTTACAATTCACAATTCACAATTCACAATTCACAATTCACAATTCACAAACCGTTACCCAACCCGAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCTTGACCCTTGACCCAACCCGTTGACCCTTGACCTTGACCTTTGACCTTTGACCTTTACTTTACTTTACTTTACTTTACTTAC	2540  ATTICANTA TANAGTIAT N P N  2620  TECGTCAAG ACGCAGTTC C V K  2700  ECCTAGCAYA EGGATCGTRI P S X  2780  ATTICACACA AACGTGTGT	2550 TGTGGAAGA ACACCTTCT H W K  2630 CTGGACGTC SAGCTGCAG L D V  2710 AACAATGAC TTGTTACTT N N E  2790 CCTGGAGGGGGGACCTCCC	ATRACA TAYTGT N X> 2640 GGCGAT CCGCTA G D> 2720 CAACT GTTGA Q L> 2800 CAAAGR TTTCY
AGACAAAGACHCH TCTGTTTCTTGHGF D K E X  2570 C TGGTGGAHCAGATG ACCACCTKGTCTAC J V X Q H  2650 CCCTATTTCTCCGTC TGGATAAAGAGGCAA A Y P S V  2730 CAAAGGCGAAGCCAT TTTCCGCTTCGGTT K G E A 1	95 (32) PACCECCTTY PTGGGGGGAAR Y P P X PIV 91-120 CAMGAAGACR GTKCTTCTGY. X R D : 2660 GCCTCTCGGATI CGGAGACCTAT P L D 2740 PSCATGGCCAR ASGTACCGGTI C B G Q	2510  CAGCCAGCCTCAA CTCGGTCGGAGTT  A S L K  CAGCCAGCCTCAA CTCGGTCGAGTT  ATACCTCACTAT AATAGAGTGATA ATAGAGTGATA ATAGAGTGATA ATAGAGTGATA ATAGAGTGATA ATAGAGTGATA ATAGAGTGAT A X F R  2750 PO ACTGGATTGCTCA CACYTAACGAGT V X C S	2520 .  GTCCCTGTT CAGGGACAA CCCTGGTTT N D Q  (51) AAGTATACC TCATATGG K Y T  DI 751-78 CCCAGGCAT P G I	2530 PTCCCAATGADA AACCGTTACTGT P G N D  2610 AGCCTCAAGCCT CGGAGTTCGGA S L K P  2690 AGCTTCACAAT CGAAAGTGTTAI A P T I  30 (84) TTCGCAACTGGA AACCGTTGACCT	2540  ATTICANTA TANAGTTAT N P N  2620 TGCGTCAAG ACGCAGTTG C V K  2700 CCCTAGCAY/ GGGATCGTRT P S X  2780  ATTGCACACA ACACGTGTGT ATTGCACACACA ACACGTGTGT C T H	2550 TGTGGAAGA ACACCTTCT H W K  2630 TTGGACGTCGACGTCGACGTGCAGCTGCAGCTGCAGCGCGACCTCCCCCCCC	ATRACA TAYTGT N X>  2640 CCCCGAT CCCCTA G D>  2720 CCAACT GTTGA Q L>  2800 CAAAGR TTTCY EX
AGACAAAGAACNCT TCTGTTTCTTGNGF D K E X  2570 ( TGGTGGAMCAGATG ACCACCTKGTCTAC Y X Q N  2650 CCCTATTTCTCCGTT TGGATAAAGAGCCAA A Y P S V  2730 CAAAGGCGAAGCCAT TTTCCGCTTCGGTT	95 (32) PACCECCTTY PTGGGGGGAAR Y P P X PINV 91-120 CAMGAAGACR GTKCTTCTGY X E D : 2660 GCCTCTGGATT CGGAGACCTA P L D 2740 PSCATGGCCAA	2510  CAGCCAGCCTCAA CTCGGTCGGAGTT  A S L K  CAGCCAGCCTCAA CTCGGTCGAGTT  ATACCTCACTAT AATAGAGTGATA ATAGAGTGATA ATAGAGTGATA ATAGAGTGATA ATAGAGTGATA ATAGAGTGATA ATAGAGTGAT A X F R  2750 PO ACTGGATTGCTCA CACYTAACGAGT V X C S	2520 .  GTCCCTGTT CAGGGACAA CCCTGGTTT N D Q  (51) AAGTATACC TCATATGG K Y T  DI 751-78 CCCAGGCAT P G I	2530 PTCCCAATGACAACCCTTACTGT PGND 2610 AGCCTCAAGCCT AGCGATTCGGA SLKP 2690 AGCTTCACAATCCGAAAGTGTTACAAATCCGAAAGTGTTACAATTCACAATTCACAATTCACAATTCACAATTCACAATTCACAAACCGTTACCCAACCCGAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCAACCCGTTGACCCTTGACCCTTGACCCAACCCGTTGACCCTTGACCTTGACCTTTGACCTTTGACCTTTACTTTACTTTACTTTACTTTACTTAC	2540  ATTICANTA TANAGTTAT N P N  2620 TGCGTCAAG ACGCAGTTG C V K  2700 CCCTAGCAY/ GGGATCGTRT P S X  2780  ATTGCACACA ACACGTGTGT ATTGCACACACA ACACGTGTGT C T H	2550 TGTGGAAGA ACACCTTCT H W K  2630 CTGGACGTC SAGCTGCAG L D V  2710 AACAATGAC TTGTTACTT N N E  2790 CCTGGAGGGGGGACCTCCC	ATRACA TAYTGT N X> 2640 GGCGAT CCGCTA G D> 2720 CAACT GTTGA Q L> 2800 CAAAGR TTTCY
AGACAAAGAACACTICTGTTTCTTCAGE D K E X  2570 C  GGGTGGAHCAGATG ACCACCTKGTCTAC I V X Q N  2650  GCCTATTTCTCCGTT GGATAAAGAGGCA A Y P S V  2730  AAAGGCGAAGCCAT TTTCCGCTTCGGTT K G E A 2  2810	95 (32) PACCECCTTY PTGGGGGGGANR Y P P X PINV 91-120 CAMGANGACR GTKCTTCTGY X B D : 2660 GCCTCTGGATT CGGAGACCTAT P L D 2740 PSCATGGCCAA SGTACCGGTT ( B G Q) 2820	2510  AGECAGCCTCAR ATCEGTCGGAGTT  A S L K  D (143)  TTATCTCACTAT ANTAGAGTGATA  X I S L C  POI 256-285  RARRCTTCAGAI  TTYYGAAGTCT  X X P R  2750 PO  AGTGRATTGCTCA  CACYTAACGAGT  V X C S  2830 2	2520 .  GTCCCTGTTT CAGGGACAN CCCTGGTTT N D Q  (51) AAGTATACC TCATATAGG K Y T  DI 751-78 CCAGGCAT CGTCCGTAL P G I	2530 TTGGCAATGADA AACCGTTACTGT P G N D  2610 AGCCTCAAGCCT TCGGAGTTCGGA S L K P  2690 AGCTTTCACAATG CGAAAGTGTTA A P T I  30 (84) TTGGCAACTGGA AACCGTTGACCT W Q L I  30 (166-195	2540  ATTTCAATA TAAAGTTAT N P N  2620 TGCGTCAAG ACGCAGTTG C V K  2700 CCCTAGCAY/ GGGATCGTRY P S X  2780 ATTGCACACA CAACGTGTGTGT C T H  (45)	2550 TGTGGAAGA ACACCTTCT H W K  2630 TCGACGTCGAGGCTGCAGG L D V  2710 AACAATGAC TTGTTACTC N N E  2790 CCTGGAGGG GGACCTCCC L E G	ATRACA TAYTGT N X> 2640 CCCCAT CCCCTA G D> 2720 CAACT GTTGA Q L> 2800 CAAACR TTTCY EX
AGACAAAGAACNCT TCTGTTTCTTCNGF D K E X  2570 E TGGTGGANCAGATC A V X Q N  2650 ECCTATTTCTCCGTT TGGATAAAGAGCCA A Y P S V  2730 EAAAGGCGAAGCCAT TTTCCGCTTCGGTZ K G E A J  2810  TATCCCTAAGGTCA	95 (32) PACCECCTTY PTGGGGGGAAR Y P P X PINV 91-120 CAMGAAGACR GTKCTTCTGY X E D : 2660 SCCTCTGGATT CGGAGACCTA P L D 2740 PSCATGGCCAA ASGTACCGGTT C B G Q 2820 AGCAATGGCC	2510  CAGCCAGCCTCAA TCGGTCGGAGTT  A S L K  O (143)  TTATCTCACTAT AATAGAGTGATA  X I S L V  POI 256-285  RAARRCTTCAGAI TTYYGAAGTCT  X X P R  2750 PO AGTGRATTGCTCA CACYTAACGAGT  V X C S  2830 2  TCTGACAGAGGA	2520 GTCCCTGTTTCAGGGACAAACCCCTGGTTTTN D Q  (51) AAGTATACCCTCATATGGCKYTCATATGGCKYTCATATGGCKYTCATATGGCKYTCATATGGCKYTCATATGGCTCCGTAACCCTGCTAACCCTGCTAACCCTGCTAACCCTGCTAACCCTGCTAACCCTGCTAACCCTGCTAACCCTGCTAACCCTGCTAACCCTGAACCCTAACCCTGAACCCTAACCCTGCTAACCCTGAACCTGAACCTGAACCTGAACCTGAACCCTGAACCTGAACCCTGAACCTGAACCTGAACCTGAACCTGAACCTGAACCTGAACCCTGAACCTGAACCTGAACCTGAACCTGA	2530 PTGCCAATGADAACCGTTACTGT P G N D  2610 AGCCTCAAGCCT AGGCATTCGGA S L K P  2690 AGCTTCACAATTCGGAAGTGTTACAATTCGGAAAGTGTTACAATTCGGAAAGTGTTACACTTGACCTTGACCTTGACCTTGACCTTGACTGAACCGTTGACCTTGACTGAAGTGTCACTGAACCGTTGACCTTGACTGAACCGTTGACCTTGACTGAACCGTTGACCTTGACTGAACCGTTGACCTGAACCGTTGACTGAACCGTTGACTGAACCGTTGACCTGACTGA	2540  ATTICANTA TANAGTIAT N P N  2620  TECGTCAAG ACGCAGTTC C V K  2700  ECCTAGCAYA EGGATCGTRI P S X  2780  ATTICACACA ANACGTGTGT C C T H  (45)	2550 TGTGGAAGA ACACCTTCT H W K  2630 TCGACGTCC SAGCTGCAGC L D V  2710 AACAATGAC TTGTACTACT N N E  2790 CCTGGAGGG GGACCTCCC L E G  2870 MAGAGATGG	ATRACA TAYTGT N X> 2640 GGCGAT CCGCTA G D> 2720 CAACT GTTGA Q L> 2800 CAAAGR TTTCY EX> 2880 AGVAA
AGACAAAGAACNCT TCTGTTTCTTCNGF D K E X  2570 ( TGGTGGAMCAGATC A V X Q N  2650 CCCTATTTCTCCGTC GGATAAAGAGCCAA A Y P S V  2730 CAAAGGCGAAGCCAT TTTCCGCTTCGGTT K G E A 3  2810 TATCCCTAAGGTCA ATAGGGATTCAGGTCA	95 (32) PACCECCTTY PACCECCTTY PACCECCTTY PACCECCTTY PACCECCTTY PACCECCTT PACCECCT PACCECC	2510  CAGCCAGCCTCAA TCGGTCGGAGTT  A S L K  O (143)  TTATCTCACTAT AATAGAGTGATA  X I S L V  POI 256-285  RAARRCTTCAGAI TTYYGAAGTCT  X X P R  2750 PO AGTGRATTGCTCA CACYTAACGAGT  V X C S  2830 2  TCTGACAGAGGA	2520 .  GTCCCTGTTT CAGGGACAAA CCCTGGTTTI N D Q  (51) AAGTATACC TCATATGC TCATATGC TCATATGC P G I  840 P  AAAGATTAATT TTCTAATT	2530 PTCCCAATGADA AACCGTTACTGT P G N D  2610 AGCCTCAAGCCT AGCGTTCACAATGAC S L K P  2690 AGCTTCACAATT CGAAAGTGTTAC A P T I  30 (84) TTGGCAACTGGA AACCGTTGACCT W Q L I  300  166-195	2540  ATTICANTA TANAGTTAT N P N  2620  TGCGTCAAG ACGCAGTTG C V K  2700  CCCTAGCAYA GGGATCGTRT P S X  2780  ATTGCACACA ACACGTGTGT C T H  (45) CHGATTTGCA KCTAAACGT	2550 TGTGGAAGA ACACCTTCT B W K  2630 TGGACGTC SAGCTGCAG L D V  2710 MACAATGAC TTGTTACTC N N E  2790 CCTGGAGGG GGACCTCCC L E G  2870 MAGAGATGC KTCTCTACC	ATRACA TAYTGT N X> 2640 GGCGAT CCGCTA G D> 2720 CAACT GTTGA Q L> 2800 CAAAGR TTTTCY EX> 2980 AGVAA TCBTT

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2890 2900 2910 2950 2960 pol 331-360 (56) CTCCCTTTCTAATCCTACCTGCGGGTGCACCCGGGGCCTCTAACCGGTTGTATCCYGGTTTTAGCTTCTCGA
E G K I S M D D L Y V G S D L E I G Q H R X K I E E L> 2970 2990 3000 3030 3040 pol 616-645 (75) CAGGSMACACCTCCTGARATGGGGCTCACCGAMACCACAAACCACAAAGACTGAGCTCCAHGCTATCCAWCTGGCTCTGC GTCCSKTGTGGAGGACTYTACCCCTGAGTGGCTKTGGTGTTTGGTTTTCTGACTCGAGGTKCGATAGGTWGACCGAGACG
R X H L L X W G L T X T T N Q R T E L X A I X L A L> 3050 3060 3070 3080 3090 pol 796-825 (87) AAGACTCCGCTYAGAGGTCAACATTGTGACAGAGATTCCCGCTGAGACTGGTCAAGAGACCGCCTATTTCHTTCTGAAA THITGAGGCCGARTCTCCAGITGTAACACTGTCTCTAACGCGCGACTCTCTCACCAGITCTCTCGCGGATAAAGKAAGACTITT Q D S G X B V N I V T D I P A E T G Q E T A Y P X L K> 3150 3160 3170 CTGCTGGCAGATGGCCTGTGARARYCATTCACACAGACAATGGGAGGACAAAGATTGAGGAACTGAGASHGCATCTGCT GACCGACCGTCTACCGGACACTYTYRGTAAGTGTGTCTGTTACCCTCCTGTTTCTAACTCCTTGACTCTSKCGTAGACGA
L A G R W P V X X I H T D N G R T X I E E L R X H L L> pol 346-375 (57) 3230 3240 3250 3260 3270 WGFTTPDKKHQKEPPFL 3290 3320 3330 vif 166-192 (111) spacers 3360 atargtggaacraacccagaaaaycaagggacrcagagraaatcacacaatgaatggccatgctgccagagtcccag TATYCACCTTGYTTGGGGTCTTTTRGTTCCCTGYGTCTCYTTTAGTGTGTTACTTACCGGTACGACGCTCTCAGGGTC D X W N X P Q K X K G X R X N H T M N G H A A T E S Q> 3370 3380 3410 3420 3430 3440 env 435-464 (165) AATCAGCAAGACAGAAACGAAMAGGAMCTGCTGGMGCTCGACAAATGGGCAAGCCTCTGGAATTGGTTTRACATTASC TTAGTCGTTCTGTCTTTGCTTKTCCTKGACGACCKCGAGCTGTTTACCCGTTCGGAGACCTTAACCAAAYTGTAATSC NQQDRNEXXLLXLDRWASLWNWFXIX 3470 3450 gag 121-150 (9)  ${\tt CACCGGARTAGCTCCHAAGTGTCCCAGANTTACCCTATCGTCCAGANTSYCCAAGGCCAAATGGTCCACCAASCCHTCT}$ GTGCCCTTYATCGAGGKTTCACAGGGTCTTAATGGGATAGCAGGTCTTASRGGTTCCGGTTTACCAGGTGGTTSGGKAGA T G X S S X V S Q N Y P I V Q N X Q G Q N V H Q X X> 3550 3530 3540 3560 3590 3600 env 480-509 (168) CCCCCAGACTCRTCGGACTGAGAATCRTTTTCGCTGTGCTCAGCATTRTCAATAGGGTCAGGCCAAGGCTATAGCCCTCTG GGGGGTCTGAGYAGCCTGACTCTTAGYAAAAGCGACACGAGTCGTAAYAGTTATCCCAGTCCGTTCCGATATCGGGAGAC SPR<sup>I</sup>LXGLRIXPAVLSIXNRVRQGYSPL> 3610 3620 3630 3640 3650 vif 106-135 (107 TCCTTCCAAACCCTCMYCTCATCCATCTGYAWTACTTTGACTGTTTCKCTGACTCCRCCATTAGGAGAGCCATCCTGGG AGGAAGGTTTGGGAGKRGGAGTAGGTAGACRTWATGAAACTGACAAAGHGACTGAGGYGGTAATCCTCTGGTAGGACCC S F Q T L X L I H L X Y F D C F X D S X I R R A I L G> 3710 3720 3730. 3700 ACASAKAGTGAGHAGGAGATGCGAAYAGCTGTGGGAHTCGGAGCCATGWTCYTTGGCTTCTGGGTGCCGCTGGCTCCA TGTSTMTCACTCKTCCTCTACGCTTATCCGACACCCTKAGCCTCGGTACWAGRAACCGAAGGACCCACGGCGACCGAGGT X X V X R R C E Y A V G X G A H X X G P L G A A G S> 3790 3800 3810 3820 3830 3840 env 300-329 (156) CCATGGCCGCTGCCTCCATSACACTGACAGTGCAAGCCTATGACCCTAGCAAAGACCTCRTTGCTGAGATTCAGAAACAG GGTACCCGCGACGGAGGTASTGTGACTGTCACGTTCGGATACTGGGATCGTTTCTGGAGYAACGACTCTAAGTCTTTGTC
T H G A A S X T L T V Q A Y D P S K D L X A B I Q K Q>

**A5** 

PHENIRE 15 (Cont)

**SUBSTITUTE SHEET (RULE 26)** 

A5 join

**A6** 

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pol 466-495 (65) 3870 3880 3890 3900 3910 3920 GGTCAGGRTCAGTGGACATWTCAGATTTWCCAAGAGCCTTTCAAAAAAGGGAACCGTCCTGGTCGGCCCTACACCCGTCAA CCAGTCCYAGTCACCTGTAWAGTCTAAAWGGTTCTCGGAAAGTTTTTTCCCTTGGCAGGACCAGCCGGGATGTGGGCAGTT G Q X Q W T X Q I X Q E P F K N I G T V L V G P T P V N> 3930 3960 pol 121-150 (42) 3970 3980 3990 4000 CATCATCGGAAGGAACHTGCTGACACAGHTTGGCYGCACCCTCAACTTTCCCATTAGGAAAGGCAGCCCTGCTATCTTTC GTAGTAGCCTTCCTTGKACGACTGTGTCKAACCGRCGTGGGAGTTGAAAGGGTAATCCTTTCCGTCGGGACGATAGAAAG
I I G R N X L T Q X G X T L N F P I S K G S P A I F> 4050 pol 301-330 (54) AGTCCAGCATGHCAHAGATTCTGCACCCTTTTAGGAWAMAAAACCCTGASATGGTCATCTATCAGTATGGTGGAGACCTCGGAAAATCCTWTKTTTTGGGACTSTACCAGTAGATAGTCATAGGGAGAC Q S S M X X I L E P P R X X N P X M V I Y Q Y P 4100 . 4110 4090 nef 136-165 (188) 4140 4150 ACATTCGGATGGTGTTTCAAACTGGTCCCCGTGGACCCCAGSGAAGTGGAAGAGRYCAACRAGGGCGAAAACAATTGCCT TGTAAGCCTACCACAAAGTTTGACCAGGGGCACCTGGGGTCSCTTCACCTTCTCYRGTTGYTCCCGCTTTTGTTAACGGA T P G W C P K L V P V D P X E V E E X N X G E N N C L> 4170 4190 4200 4180 pol 271-300 (52) CCTCTTTAGGAAATACACAGCCTTTACCATTCCCTCCAYCAATAACGAAACCCCTGGCATTAGGTATCAGTATAACGTCC GCM ANATOCTTTATGTCTCGGANATGGTANGGGAGGTRGTTATTGCTTTGGGGACCGTNATCCATAGTCATATTGCAGG PRKYTAFTIPSX NNETPGIRYQYN V> 4270 4280 4290 env 315-344 (157) TECCTCAGGGATGGGAAGCACAATGGGAGCCGCCAGCATKACCCTCACCGTCCAGGCTAGGCMACTGCTCAGCGGAATC ACCCACTCCCTACCCCTTCGTGTTACCCTCGGCGGTCGTAMTGGGAGTGCCAGGTCCGATCCGWTGACGAGTCGCCTTAG L P Q G W G S T H G A A S X T L T V Q A R X L L S G I> 4350 4370 pol 451-480 (64) 4360 GTCCAGCAACAGARCAATCTGCTGGGGGAAATAGGGAAATCCTCARAGAGCCTGTGCATGGGGTCTACTACGATCCCTC
CAGGTCGTTGTCTYGTTAGACGAGCKCCTCTTATCCCTTTAGGAGTYTCTCGGACACGTACCGCAGATGATGCTAGGGAG
V Q Q Q X N L L X E N R E I L X E P V H G V Y Y D P S> 4450 4410 4420 4430 4440 vpu 61-81 (136) 4480 CAAGGATCTGRTCGCTGAAHTCCAAAAGCAAGGCASACAGGAACTGTCCRCCWTGGTGGATATGGGAAACTACGACCTCG GTTCCTAGACYAGCGACTTYAGGTTTTCGTTCCQTSTCTCCTTGACAGGYGGWACCACCTATACCCTTTGATGCTGGAGC K D L X A E X Q K Q G X E E L S X X V D H G N Y D L> spacers 4510 4520 4530 vpr 61-90 (116) GAGTGGACANTAACCTGCCGCTATTAGAAYCCTGCAACAGCTCHTGTTCACTTTAGGATTGGCTGCCRGCACTCC CTCACCTGTTNTTGGACGGCGGTNATCTTRGGACGTTGTCGAGKACAAGYAAGTGAAATCCTAACCGACGGYCGTGAGG G V D N N L A A I R X L Q Q L X P X H F R I G C X H S> 4610 4580 4590 gag 406-435 (28) 4570 4600 AGGATTGCCATCHYCCGTCAGAGAGGGGCACACCACGAAAAAAGGGATGCTGGAAGTGTGGCARAGAGGGACACCA TCCTAACCGTACKRGGCAGTCTCTTCCCSGTCCGAGGGTCCTTTTTCCCTACGACCTTCACACCGTYTCTCCCTGTGGT
R I G I X R Q R R X R A P R K K G C W K C G X B G H Q> 4650 4660 4680 4690 4720 GATGAAGGATTGCACTGAGAGACAGGCTAACTTTCTGGGAAAGGAWGCCAGACTGRTTATCARAACCTATTGGGGACTGC
CTACTTCCTAACGTGACTCTGTCCGATTGAAAGACCCTTTCTTWCGGTCTGACYAATAGTYTTGGATAACCCCTGACG
H K D C T E R Q A N P L G K X A R L X I X T Y W G L> . 4780 4760 4770 vif 61-90 (104) ATACCGGTGAGAGAGACTGGCASCTCGGCCAMGGCGTCAGCATTGAGTGGAGGAYAAGGGAAAGGGCTGAGGATAGCGGC TATGGCCACTCTCTCTGACGTSGAGCCGGTWCCGCAGTCGTAACTCACCTCTTTTCCCGACTCCTATCGCCG
H T G E R D W X L G X G V S I E W R X R E R A E D S G>

# FIGURE 15 (Cont)

**SUBSTITUTE SHEET (RULE 26)** 

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**A6** 

**A7** 

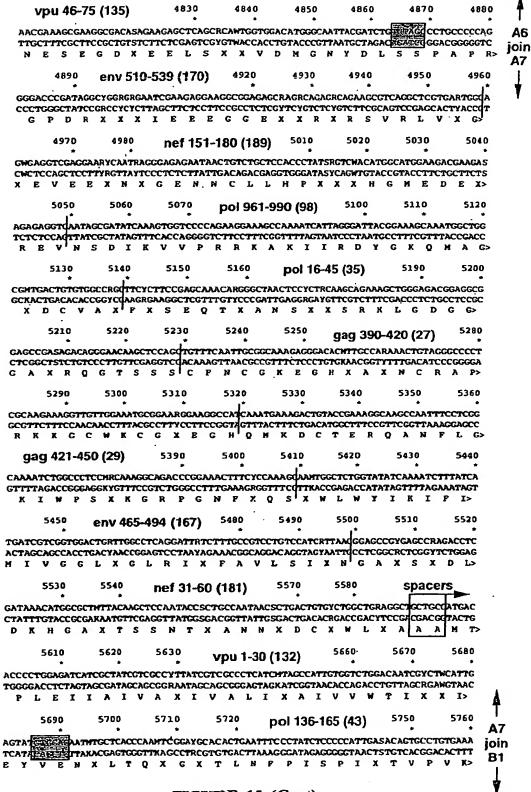
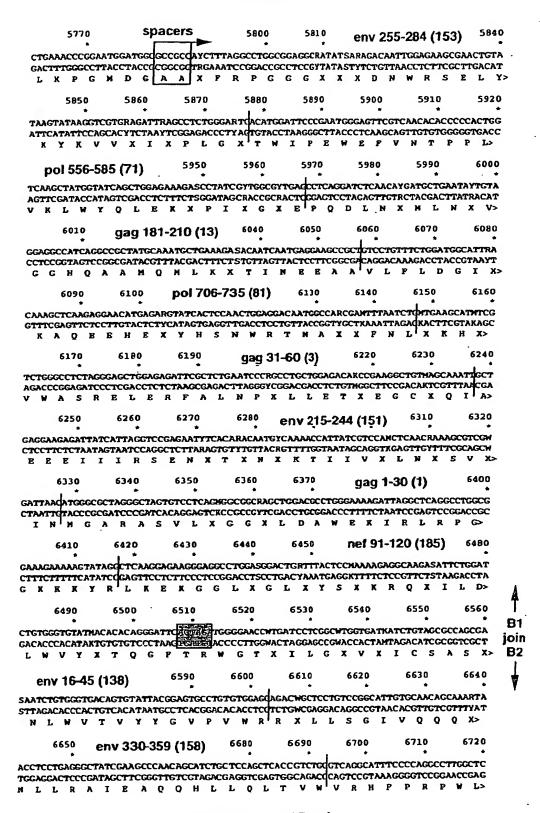


FIGURE 15 (Cont) **SUBSTITUTE SHEET (RULE 26)** 



6770 6780 6790 6800 vpr 31-60 (114) 6760 CACRRCCTGGGACAGYACATCTATGAGACATACGGAGACACATGGKMGGGAGTGGAAGCCCTCAAAGCCCTCATCAHACC GTGYYGGACCCTGTCTTGTAGATACTCTGTATYCCTCTGTGTACCHKCCCTCACCTTCGGGAGTKTCGGGAGTAGTKTGG H X L G Q X I Y E T Y G D T W X G V E A L X A L I X P> 6810 6840 6850 6860 6870 6880 . vif 151-180 (110) CAAAAAGATTARGCCTCCCCTCCCATCCGTGAAAAAGCTCACCGAAGACARATGGAATRAGCCTCAAAAGAYATATAGCG GTTTTTCTAATYCGGAGGGAGGGTAGGCACTTTTTCGAGTGGCTTCTGTYTACCTTAYTCGGAGTTTTCTRTATATCGC K K I X P P L P S V K K L T E D X W N X P Q K X Y S> 6890 6900 6930 pol 901-930 (94) CTGGCGAAAGGATTRTCGATATCATTGCAWCCGACATTCAGACTAAGGAACTGCAAAASCAAATCHYAAAGATTCAGAAT GACCGCTTTCCTAAYAGCTATAGTAACGTWGGCTGTAAGTCTGACTTTTGCGTTTTAGKRTTTCTAAGTCTTA AGERIXDIIAXDIQTKELQXQIXKIQN> 7040 6970 6980 6990 pol 886-915 (93) 7020 PAVPIHNPKRKGGIGGYSAGERIX DI I> 7070 7080 7110 7120 7060 . gag 256-285 (18) 7050 CGCCASCGATATCRTTCCCGTGGGCGAWATCTATAAGAGATGGATGATCATTCTGGGACTCAACAAAATCGTGAGAATGTATY
GCGGTSGCTATACYAAGGGCACCCGCTWTAGATATTCTCTACCTAGTAAGACCCCTGAGTTGTTTTAGCACTCTTACATAR
A X D I X P V G X I Y K R W I I L G L N R I V R M V 7130 7140 7150. 7160 7170 env 495-524 (169) MACCGTCAGCATTCTGGATATCAGAGTGAGACAGGGATACTCCCCCCTCAGCTTTCAGACACTGNYGCCCGCTCCCAGA RTGGGCAGTCGTAAGACCTATAGTCTCACTCTGTCCCTATGAGGGGGGAGTCGAAAGTCTGTGACKRCGGGCGAGGGTCTX P V S I L D I R V R Q G Y S P L S P Q T L X P A P R> 7230 7240 7250 7260 7270 7280 7220 GGCCTGACAGACYCGRASGCATTGAGGAAGACTCCAGSCAGGACCATCAGTATCCCATTYCCGAACAGCCTCTGYCTCA CCGGGACTGTCTGRGCYTSCGTAACTCCTTCTGAGGTCSGTCCTGGTAGTCATAGGGTAARGGCTTGTCGGAGACRGAGT
G P D R X X X I E E E S X Q D H Q Y P I X E Q P L X Q> 7310 7320 7330 7340 tat 61-90 (122) GMCAAGGGGAGRCAATCCCACAGRCCCTRAGGAAAGCAAAAAG GGGGGGGGGGGGGCCCATGAATAAGGAACTGA B<sub>2</sub> CKGTTCCCCTCYGTTAGGGTGTCYGGGAYTCCTTTCGTTTTTC CCCCCCCCCCCCCCCCCCCACCTAATTCCTTGACT JOIN G V V E S H N K E L> X R G X N P T X P X E S K K **B3** 7400 7410 7420 7430 7440 7370 pol 856-885 (91) TTTTCTAATACCCTCTCCAGTCCCTKGTCCGACTCGTGGACTTTTGGCGACACGTTTACTGACGGTACGTCTACGAGTTC KIIGQVRXQAEHLKTAVQH<sup>I</sup>AAMQHLK> 7450 · 7460 gag 196-225 (14) 7490 7500 7520 GAWACCATTAACGAAGAGGCTGCCGAGTGGGACAGARTCCATCCCGTCCATGCCGGACCCRTTSCCCCTCTCACCGHGAT CTWTGGTAATTGCTTCTCCGACGGCTCACCCTGTCTYAGGTAGGCCAGGTACGGCCTGGGYAASGGGAAGTGGCKCTA
X T I N E E A A E W D R X H P V H A G P X X P L T X I> 7580 7550 7530 pol 181-210 (46) TTGTAHAGAANTGGAAVAAGAAGECAAAATCTCCARGATTGGCCCTGAGAATCCCTATAACACACCCRTCTTTGCCATTC AACATKTCTTTACCTTBYTCTTCCGTTTTAGAGGTYCTAACCGGGACTCTTAGGGATATTGTGTGGGYAGAAACGG7A/G C X E N E X E G K I S X I G P E N P Y N T P X P A I 7670 pol 871-900 (92) 7610 7620 7630 7640 Q V R X Q A E H L K T A V Q M A V P I H N P X R X G G>

# EEGURE 15 (Cont)

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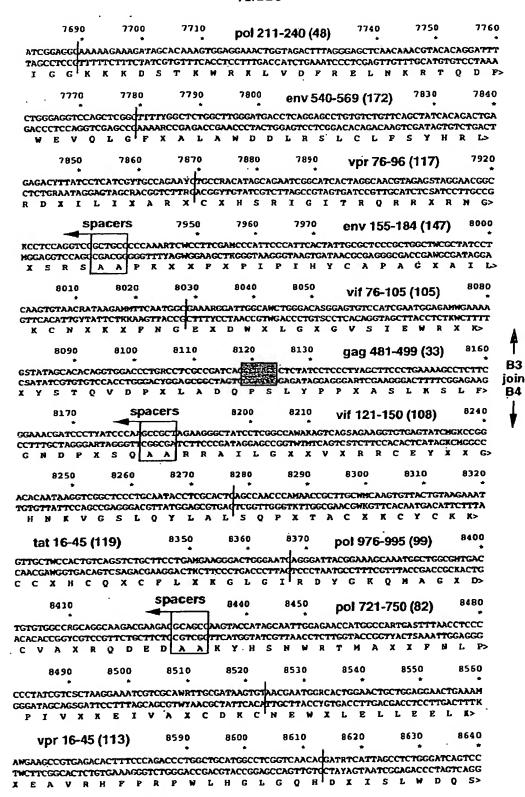


FIGURE 15 (Cont)
SUBSTITUTE SHEET (RULE 26)

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8650 8680 8690 8700 8710 env 106-144 (144) CTGAAACCCTGTGTGAAACTGACACCCCTCTGCGTCACCCTCAACTGTACCAATGCCAATCTCHHGAAGAGHTACTCCAC GACTTTGGGACACACTTTGACTGTGGGGAGACGCAGTGGGAGTTGACATGGTTACGGTTAGACHCTTCTCKATGAGGTG LKPCVKLTPLCVTLNCTNANLIXXXX S T> 8730 8740 8770 8780 vif 91-120 (106) 8790 8800 CCAAGTGGACCCCGRTCTGGCTGACCAWCTGATTCACCTCCACTATTTCGATTGCTTTKCCGATAGCRCAATCCAATCCCA CGTTCACCTGGGGCYAGACCGACTGGTWGACTAAGTGGAGGGTGATAAAGCTAACGAAANGGCTATCGYGTTAGGTAAGGGT Q V D P X L A D X L I H L H Y F D C F X D S X I H P> 8810 8820 8830 nef 166-195 (190) TSRGCCWACACGGAATGGAGGATGAGGAWAGGGAAGTGCTGAWATGGAAATTCGATAGCCRTCTGGCTCKCAGCCATATS ASYCGGWTGTGCCTTACCTCCTWTCCCTTCACGACTWTACCTTTAAGCTATCGGYAGACCGAGHGTCCGTATAS XXX H G M E D E X R E V L X W K F D S X L A X R H X> 8900 8890 8910 8920 pol 151-180 (44) 8950 8960 GCTATEGAWACCGTCCCCGTCAAGCTCAAGCCTGGCACGGACCCAAAGTGAAACAGTGGCCCCTCAC CCITATION OF THE SECRET CONTROL OF THE SECRET PIXT V P V K L K P G M D G P K V K Q W P L T> 8970 8980 8990 9000 gag 436-465 (30) CGAAGAGAAAATCAAAGCCGATTTGGCCTAGCMRCAAGGGAAGGCCTGGCAATTTCCYGCAGTCCARGCCTGAGCCTACCGGCTCTCTTTTTAGTTTCGGTAAACCGGATCGKYGTTCCCTTCCGGACCGTTAAAGGRCGTCAGGTYCGGACTCCGATGGC EEKIKAI W PS X K G R P G N P X Q S X P E P T> 9060 9070 9050 9080 9090 vif 31-60 (102) CACCCCAGCCGAGARCTTTRGATTCGGGATTAGCAAAAAGGCTAASGGATGGTTTTACAGACACCATTMCGAMAGCCRA GTGGGGGTCGCCTCTYGAAAYCTAAGCCGTAATCGTTTTTCCCATTSCCTACCAAAATGTCTGTGGTAAGCCTWTCGGYTAPPPAEXPGISKKAXGWPYRHHXXSS> 9130 9140 9150 9160 9170 9180 CACCTAAGGTCAGGTCCGAGGTCCACATTCCCCTCGGGATGATGACGGCTTGCCAAGGCGTCGGGGGACCCRGTCACAA GTGGGATTCCAGTCGAGGCTCCAGGTGTAAGGGGAGCCCTTACTACTGCCGAACGGTTCCGCAGCCGCCCCCCTGGGYCAGTGTT H P K V S S E V H I P L G H M T A C Q G V G G P X H K> gag 346-375 (24) 9230 9240 9250 9260 9270 9280 AGCCAGGGTACTGGCAGAGGCTATGTCCCAGGYGAMCHACGCTAACATTCCTCCCATTGTGSCCAAAGAGATTGTGGCAN TCGGTCCCATGACCGTCTCCGATACAGGGTCCTCTKGKTGCGATTGTAAGGAGGGTAACACCGTW ARVLAEAMSQXXXANIPPIVXKEIVA> 9290 pol 736-765 (83) 9320 9330 9340 9350 9360 RCTGTGACAAATGCCAGCTCAAGGGTGAGGCTATKCACCGACAGGTGRACTGTAGCCCTTCCGAGGGAWCAAGACAGRCCT YGACACTGTTTACGGTCGAGTTCCCACTCCGATAMGTGCCTGTCCACYTGACATCGGGAAGGCCTCCCTTMGTTCTGTCYGA X C D X C Q L X G E A X H G Q V X C S P S E G X R Q X> 9370 9380 rev 31-60 (126) 9410 9420 AGGARGAACAGACGTAGAAGGTGGCGTGHGAGGCAAAGGCAAATCCRCKCCATCTCCGAGWGGATTCTGGGACAGATRAG TCCTYCTTGTCTGCATCTTCCACCGCACKCTCCGTTTCCGTTTAGGYGHGGTAGAGGCTCWCCTAAGACCTGTCTAYTC R X N R R R W R X R Q R Q I X X I S E X I L G Q X R> 9450 9460 9470 gag 226-255 (16) GGAACCCAGAGGCTCCGACATTGCCGGTACCACAGGCACACTGCAAGAGCAAATCGSATGGATGACAARCAATCCCCCTR CCTTGGGTCTCCGAGGCTGTAACGGCCATGGTGTTCGTGTGACGTTCTCGTTTAGCSTACCTACTGTTYGTTAGCGGGAY EPRGSDIAGTTSTLQEQIXWNTXN 9530 9540 9550 pol 841-870 (90) RCATTMAGCAAGAGTTTGGCATTCCCTATAACCCTCAGTCCCAGGCGTCGTGGAAAGCATGAACAAAGAGCTCAAGAAA YGTAAKTCGTTCTCAAACCGTAAGGGATATTGGGAGTCAGGGTCCCGCAGCACCTTTCGTACTTGTTTCTCGAGTTCTTT

**B4** 

join

**B**5

FIGURE 15 (Cont)

**SUBSTITUTE SHEET (RULE 26)** 

XIX QEFCIPYNPQSQCVVESHNKELK K>

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**B**5

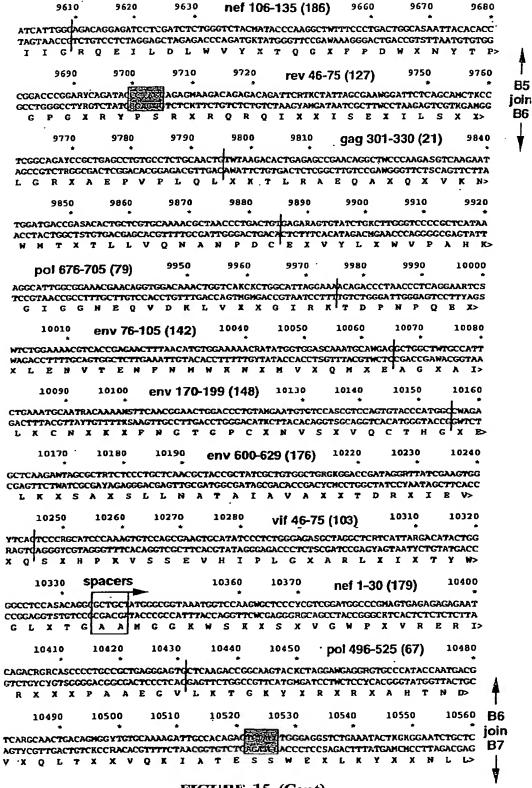


FIGURE 15 (Cont)

**SUBSTITUTE SHEET (RULE 26)** 

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10630 10620 10590 10600 10610 env 585-614 (175) CHGTACTGGGGCCHGGAACTGAAAAHCTCCGCCRTCAGCCTCCTGAATGCCACAGCGATTSHGCTGCCTGAGAAAGAHAG GHCATGACCCCGGHCCTTGACTTTTWGAGGCGGYAGTCGGAGGACTTTACGGTGTCGQTAASHCGACGGACTCTTTCTWTC X Y W G X E L X X S A X S L L N A T A I X L P E X X S 10680 10690 10700 10710 10720 10650 pcl 391-420 (60) CTGGACCGTCAACGATATCCAAAAGCTCGTGGGAAAGCTCAACTGGGCATCCCAGATTTACSCCGGAAGAGCCCATTGAGG GACCTGGCAGTTGCTATAGGTTTTCGAGCACCCTTTCGAGTTGACCCGTAGGGTCTAAATGSGGCCTTCTCGGTAACTCC W T V N D I Q R L V G K L N W A S Q I Y X G | R A I E> 10730 10770 10780 10740 env 345-374 (159) CTCAGCAACACWTGCTGCAACTGACAGTGTGGGGCATTAAGCAACTGCAAGCCAGAGTGCTCGCCRTTGAGAGATAQCTC CAGTCGTTGTCHACGACGTTGACTGTCACACCCCGTAATTCGTTGACGTTCGGTCTCACGAGCGGYAACTCTCTATCGAG AQQHXLQLTVWGIRQLQARVLAXERYL> pol 631-660 (76) 10860 10870 10880 10820 10830 10810 GCCCTCCAGGATAGCGGATYGGAAGTGAATATCGTCACCGATAGCCAATACGCTCTAGGCATCATTCWGGCTCAGCCTGA CGGGAGGTCCTATCGCCTARCCTTCACTTATAGCAGTGGCTATCGGTTATGCGAGATCCGTAGTAAGWCCGAGTCGGACT A L Q D S G X E V N I V T D S Q Y A L G I I X A Q P D> 10960 env 420-449 (164) 10950 10910 10920 10890 10900 CARAAGGGAAAGGGAAATCTCCAACTATACCARTCWGATTTACRAGATCCTCACCGAATCTCAAAATCAACAGGATAGGA CTTTCCCTTTAGAGGTTGATATGGTYAGWCTAAATGYTCTAGGAGTGGCTTAGAGTTTTAGTTGTCCTATCCT X SIEREIS NYTXXIIYXILTES Q N Q Q D R> 11000 11010 env 285-314 (155) 11040 10970 10980 10990 ATGACHAAGASCTCCTGCCTCCACAARGGCTAAGAGAAGGGTCGTGSAAAGGGAAAAGCGTGCCGTCGGCHTTGGGGCT
TACTCKTTCTSGAGGAGGGTGTYYCCGATTCTCTTCCCAGCACSTTTCCCTTTTCGCACGGCAGCCGKAACCGCGA
N E X X L L A P T X A K R R V V X R E K R A V G X G A> 11080 11090 11070 11050 11060 pol 91-120 (40) ATGWTTYTCGGATTCCTCGGCGCTGCGAAACCCAAAATGATCGGAGGCATTGGAGGCTTTATCAAAGTCAGGCAGTATGA TACWARRACCTAAGGACCCGCGACGGTTTGGGTTTTACTAGCCTCCGTAACCTCCGAAATAGTTTCAGTCCGTCATACT M X X C F L G A A R P K M I G G I G G F I K V R Q Y D> 11150 11160 11170 11180 11140 11130 CCAAATCHTTATCGAAATCTGTGGAHASAAGGCTATCTCCTACCATAGGCTCAGGGATTTCATTCTGATCGYCGCTAGGA GGTTTAGKAATAGCTTTAGACACCTKTSTTCCGATA¢AGGATGGTATCCGAGTCCCTAAAGTAAGACTAGCRGCGATCCT QIXIBICGX K A I S Y H R L R D P I L I X A R> 11270 11280 11230 11240 11250 11260 env 555-584 (173) YTGTGGAACTGCTCGGCCRTACCTCCCTGARAGGCCTCCRGAGAGGGACACTGAATGCCTGGGTGAAAGTGRTTGAGGAA RACACCTTGACGAGCCGGYATCGAGGGACTYTCCGGAGGYCTCTCCCTGTGACTTACGGACCCACTTTCACYAACTCCTT X V E L L G X S S L X G L X R G T L N A W V X V X E E> 11350 11320 11330 11340 11290 gag 151-180 (11) join K X F X P E V I P M F X A L S E G A T L E S N T X A N> C1 11420 11410 11370 11380 nef 46-75 (182) CANTSCCGATTCCGYCTGCCTCRAAGCCCAGGAAGAGGAAGRAGTGGGATTTCCTGTGAGACCCCAAGTGCCTAGAGCCK GTTASGGCTAACGCRCACCGACYTTCGGGTCCTTCTCCTTCYTCACCCTAAAGGACACTCTGGGGTTCACGGATCTCGGH N X D C X W L X A Q E E E X V G F P V R P Q V P R A> spacers 11520 11480 11490 11450 env 630-651 (178) GGAGGGCTATCCTCHACATTCCCASGAGGATTAGGCAAGGCYTTGAGAGAGCCCTCCTAGCCGCAGAATGGGATAGGRTTCCTCCCGATAGGAGAGCCCTCCTTGGGAGGATGGGATAGGATAGGATACCTATCCYAA X R A I L X I P X R I R Q G X E R A L L A A E W D R X>

### FIGURE 15 (Cont)

```
11600
                                                                11590
                                                      11580
                                            11570
                       gag 211-240 (15)
     11530
CACCCTGTGCACGCTGGCCCTRTCSCTCCCGGCCAAATSAGAGAGCCCAGGGGGAAGCGATATCGCTGGCACAACCCTCAG
GTGGGACACGTGCGACCGGGAYAGSGAGGGCCGGTTTASTCTCTCGGGTCCCCTTCGCTATAGCGACCGTGTTGGGAGTC
HPVHAGPXXPGQXREPRGSDIAGTTLR>
                                                       11660
                                                                11670
                                  nef 76-105 (184)
                         11630
               11620
     11610.
GCCCATGACATATAAGGSCGCTRTTGACCTCAGCYTGTTTCTGAAAGAGAAAGGCGGACTGGAWGGCCTCRTCTATAGCM
CGGGTACTGTATATTCCSGCGAYAACTGGAGTCGRACAAAGACTTTCTCTTTCCGCCTCACCTWCCGGAGYAGATATCGK
  P M T Y K X A X D L S L F L K E K G G L X G L X Y S>
                                                                11750
                                              vpr 1-30 (112)
                                   11720
                         11710
    spacers
AGAAAGCTGCTATGGAACAGGCTCCCGAAGACCAARGCYCTCAGAGAGAGCCTTACAATGAGTGGRCCCTGGAGCTCCTG
TCTT CGACGATACCTTGTCCGAGGGCTTCTGGTTYCGRGAGTCTCTCTCGGAATGTTACTCACCYGGGACCTCGAGGAC
  KAAMEQAPEDQXXQREPYNEWXLELL>
                                                                          11840
                                                      pol 481-510 (66)
                                  11800
                                             11810
                         11790 '
               11780
     11770
GAAGAGCTCAAGMAMGAGGCTCAAGRCCAATGGACCTWCCAAATCTWTCAGGAACCCTTTAAGAATCTGAAAACCGGAAA
CTTCTCGAGTTCKTKCTCCGAGTMCYGGTTACCTGGAWGGTTTAGAWAGTCCTTGGAAATCTTTAGACTTTTGGCCTTT
E E L K X E A Q X Q W T X Q I X Q E P P K N L K T G K>
                                                                11910
                                                       11900
                                             11890
                                   11880
                         11870
               11860
     11850
GTATKCCAGAAWGAGARGCGCTCACACAAACTGGATGACAGAWACCCTCCTGGTCCAGAATGCCAATCCCGATTGCAAGW
CATAMGGTCTTWCTCTYCGCGAGTGTGTTTCACCTACTGTCTWTGGGAGGACCAGGTCTTACGGTTAGGGCTAACGTTCW
  Y X R X R X A H T N W H T X T L L V Q H A N P D C K>
                                                       11980
                                                                11990
                                             11970
                                   11960
                         11950
  gag 316-345 (22)
CCATCCTCARGGCTCTGGGAMCCGGAGCCWCACTGGAAGAGCCTGAGGTCATCCCTATGTTCWCAGCCCTCAGCGAAGGCGCTAGGAGTYCCGAGACCCTKGGCCTCGGWGTGACCTTCTGGGACTCCAGTAGGGATACAAGWGTCGGGAGTCGCTTCCG
X I L X A L G X G A X L E E P E V I P M F X A L S E G>
                                                                          12080
                                                                12070
                                                       12060
                                             12050
              gag 166-195 (12)
                                   12040
     12010
GCTACCCCCAAGACCTGAATAYGATGCTCAACAYCGTCGGCGGACACCAATCCACCCTCCAGGAACAGATTGSCTGGAT
CGATGGGGGTTCTGGACTTATRCTACGAGTTGTRGCAGCCGCCTGTGGTTAGGTGGGAGGTCCTTGTCTAACSGACCTA
A T P Q D L N X H L N X V G G H Q S T L Q E Q I X W M>
                                                                12150
                                                       12140
                        gag 241-270 (17)
                                             12130
               12100
CACAARTAACCCTCCCRTCCCTGTCGGAGASATTTACAAAAGGTGGATTATCCTCGGCCTC
     12090
                                                                                 join
                                                                                  C2
  TXNPPXPVGXIYRRWIILGLTR
                                                                           12240
                                                                12230
                                                       12220
                                  pol 241-270 (50)
                         12190
               12180
      12170
CCGGCCTCAAGAAAAAGAAAAGCGTCACCGTCCTGGATGTGGGAGACGCTTACTTCAGCGTCCCCCTCGACRAARRQCAA
GGCCGGAGTTCTTTTTCTTTTCGCAGTGGCAGGACCTACACCCTCTGCGAATGAAGTCGCAGGGGGAGCTGYTTYYGGTT
AGLKKKKSVTVLDVGDAYFSVPLDXX
                                                                 12310
                                            pol 541-570 (70)
                                   12280
                         12270
                12260
      12250
ARGGAAACCTGGGAGRCTTGGTGGAYGGAHTACTGGCAGGCTACCTGGATTCCTGAGTGGGAGTTTGTGAATACCCCTCC
TYCCTTTGGACCCTCYGAACCACCTRCCTKATGACCGTCCGATGGACCTAAGGACTCACCCTCAAACACTTATGGGGAGG
 X E T W E X W W X X Y W Q A T W I P E W E F V N T P P>
                                                                           12400
                                                     nef 121-150 (187)
                                             12370
                                   12360
                         12350
                12340
      12330
CCTCGTCTTTCCCGATTGGCAWAACTATACCCCTGGCCCTGGCRYAAGGTATCCCCTCACCTTTGGATGGTGCTTTAAGC
GGAGCAGAAAGGCTAACCGTWTTGATATGGGGACCGGGACCGYRTTCCATAGGGGAGTGGAAACCTACCACGAAATTCG
L V F P D W X N Y T P G P G X R Y P L T P G W C F K>
                                                      pol 571-600 (72)
                                              12450
                                   12440
                          12430
                12420
      12410
 TCGTGCCTGTGGACCCCQAAACTGTGGTACCAACTGGAAAAGGAMCCCATTGYCGGAGYCGAAACCTTTTACGTGGACGGA
AGCACGGACACCTGGGGTTTGACACCATGGTTGACCTTTTCCTKGGGTAACRGCCTCRGCTTTGGAAAATGCACCTGCCT
 L. V P V D P K L W Y Q L E K X P I X G X E T F Y V D G>
```

# PIGURE 15 (Cont)

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12490 12500 12510 12520 gag 136-165 (10) 12550 12560 GCCGCCARCAGAGAGACAAAGCTCGGGCAAAACSYCCAGGGACAGATGGTGCATCAGSCTHTTAGCCCCAGGACCCTCAA CGGCGGTYGTCTCTCTTTCGAGCCGGTTTTGSRGGTCCCTGTCTACCACGTAGTCSGAKAATCGGGGTCCTGGGAGTT
A A X R E 7 K L G Q N X Q G Q M V H Q X X S P R T L N> 12570 12580 12590 12600 12610 env 61-90 (141) CGCTTCGCTCAAGGTCRTCGAAGAGAAAGSCTTTARQGAMACCGAAGTGCATAACGTCTGGGCTACCCATGCCTGTGTGC  ${\tt GCGAACCCAGTTCCAGYAGCTTCTCTTTCSGAAATY} {\tt GCTATCGCTTCACGTATTGCAGACCCGATGGGTACGGACACACG}.$ A W V R V X E E R X F X X T E V H N V W A T H A C V> 12660 12670 12650 12680 12690 12710 12700 CTACCGATCCCAATCCCCAAGAGRTTSWCCTGGAGAATGTGACAGAQCTCAAGGATCAGMAAYTCCTCGGCMTTTGGGGA GATGGCTAGGGTTAGGGGTTCTCYAASWGGACCTCTTACACTGTCTTGGGGTTCCTAGTCXTTRAGGAGCCGRAAACCCCTPTDPNPQEXXLENVTELLXDQXXLGXWG> env 375-404 (161) 12750 12760 12770 12780 TGCTCCGGCAAAHTCATTTGCACAACCRMTGTGCCTTGGAACAGCWCCTGGTCCAACCHAKCTGGCCATAACAAGTGGG acgaggccgtttkagtaaacgtgttggykacacggaaccttgtcgaggaccaggttgkthgaccggtattgttcaccc C S G K X I C T T X V P W N S X W S N I X X G H N K V G> 12810 vif 136-165 (109) 12840 12850 12860 12870 12880 AAGCCTCCAGTATCTGGCTCTGAHGGCTCTGATTAHGCCTAAGAAAATCARACCCCCTCTGCCTAGGGYTAAGACAATCA TTCGGAGGTCATAGACCGAGACTKCCGAGACTAATKCGGATTCTTTTAGTYTGGGGGAGACGGATCGCRATTCTGTTAGT S L Q Y L A L X A L I X P K K I X P P L P S X K T I> spacers 12890 12900 env 230-254 (152) 12930 12960 TTGTGCATCTGAATRAGTCCGTGGWAATCAATTGCACAAGGCCTARCAATAACACAAGGANAGCCGCC GAAGWA AACACGTAGACTTAYTCAGGCACCWTTAGTTAACGTGTTCCGGATYGTTATTGTGTTCCTX. join I V H L N X S V X I N C T R P X N N T R X A AASEX> C3 12980 12990 gag 106-135 (8) 13020 13030 CAGANWAAGTCCMANCAGAAAAACCCAGCAAGCCGCCGATACAGGCARCTCCAGCHAGGTCAGCCAAAACTATCCCAT GTCTTWITCAGGRTTGTCTTTTGGGTCGTTCGGCCGCCGCTATGTCCGTTGAGGCTCGAGTCGAGTCGATTTGATAGGGTA Q X K S X Q R T Q Q A A A D T G X S S X V S Q N Y P I> 13060 13070 13080 13050 pol 826-855 (89) TGTGTCCAACTTTACCTCCRCCRCCGCGAAAGCCGCTTGTTGGTGGGCCRRTATCMAACAGGAGTTTGGAATCCCTTACA ACACAGGTTGAAATGGAGGYGGYGACACTTTCGGCGAACAACCACCCGGYYATAGKTTGTCCTCAAACCTTAGGGAATGT S N P T S X X V K A A C W W A X I X Q E P G I P 13130 13160 13170 13200 pol 586-615 (73) ATCCCCAAAGCCA/ACATTCTATGTGGATGGCGCTGCCARTAGGGAAACCAAACTGGGAAAGGCTGGCTATGTGACAGAC TAGGGGTTTCGGTTGTAAGATACACCTACCGCGACGGTYATCCCTTTGGTTTGACCCTTTCCGACCGATACACTGTCTG N P Q S Q T P Y V D G A A X R E T K L G X A G Y V T D> 13220 13210 13230 13240 13250 pol 766-795 (85) agaggcagacagaaartcrttagqggaatctggcagctcgactgtacccatctggáaggcaaartcattctggtagccgt TCTCCGTCTGTCTTTYAGYAATCQCCTTAGACCGTCGAGCTGACATGGGTAGACCTTCCGTTTYAGTAAGACCATCGGCA R G R Q K X X S G I W Q L D C T H L B G K X I L V A V> 13300 13290 13310 13320 13330 13340 CCACGTCGCCTCCGCTACATTGAGGCTGAGGTGGCCAATGAGCAAGTGGATAAGCTCGTGAKTKCCGGAATCAGAAAGG GGGCAGGCGGAGGCCGATGTAACTCCGACTCCAGCCGTTACTCGTTCACCATTATTCGAGCACTMAMGGCCTTAGTCTTTCC
H V A S G Y I B A E V G N E Q V D K L V X X G I R X> pol 691-720 (80) 13390 13400 13410 13420 13430 13440 TGCTATTCCTCGACGGAATCRATAAGGCTCAGGAAGAGCACGA\fotcaGGGAAAGGATTAGGCRARCCSCTCCCGCTGCT ACGATAAGGAGCTCCCTTAGYTATTCCGAGTCCTTCTCGTGCTTCACTCCCTTTCCTAATCCGYTYGGSGAGGGCGACGA V L F L D'G I X K A Q E E H E'V R E R I R X X X P A A>

FIGURE 15 (Cont)
SUBSTITUTE SHEET (RULE 26)

C3

C4

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nef 16-45 (180) 13470 13490 13480 13500 13510 13520 GAAGGCGTCGGCGCTGYCTCCCRGGATCTGGATAAGKACGGAGCCHTCACCTCQACAAGCGGAACCCAACAGTCCCAGGG CTTCCGCAGCCGCGACGAGGGYCCTAGACCTATTCHTGCCTCGGKAGTGGAGGTGTTCGCCTTGGGTTCTCAGGGTCCC E G V · G A X S X D L D K X G A X T S T S G T Q Q S Q G> 13560 13570 13580 13590 13600 13530 rev 91-120 (130) AACTGAAACTGGCGTCGGCMTCCCTCAGATTTYGGGAGAGTCCAGCGYTTTCCTCGGCYCCGGTCCATCGTCATCTGGG TTGACTTTGACCGCAGCCGXYGGGAGTCTAAARCCCTCTCAGGTCGCRAYAGGAGCCGRGGCCCAAGGTAGCAGTAGACCC
T E T G V G X P Q I X G E S S X X L G X G S I V I W> spacers 13620 13650 13660 pol 526-555 (69) GTAAAACCCCTAAGTTTARGCTCCCCATTCAGARAGAGACATGGGAARCCTGGTGGAYGGASTATTGGCAAGCGCTGCT CATTTTGGGGATTCAAATYCGAGGGGTAAGTCTYTCTCTGTACCCTTYGGACCACCTRCCTSATAACCGTTCGGCGACGA G K T P K P X L P I Q X E T W E X W W X X Y W Q A A 13690 13710 env 140-169 (146) 13740 TACAGACTGATCARCTGTAACACAGCGYTATCAHACAGGCTTGCCCTAAGRTTASCTTTGASCCTATCCCTATCCATTA ATGTCTGACTAGTYGACATTGTGTTCGCRATAGTKTGTCCGAACGGGATTCYAATSGAAACTSGGATAGGGATAGGTAAT Y R L I X C N T S X I X Q A C P K X X P X P I P I H Y> 13800 pol 376-405 (59) WMGYELHPDRWTVQPIXLPEK> gag 331-360 (23) 13850 13860 13870 13880 13890 13920 ASTCCTGGACAGTGAATGACATTCAGAAAMCAATTCTGARAGCCCTCGGCKCAGGCGCTMCCTGGAGGAAATGATGACA TSACCACCTGTCACTTACTGTAAGTGTTTWGTTAAGACTYTCGGGAGCCGKGTCCGCGAWGGGACCTCCTTTACTACTGT X S W T V N D X Q X X I L X A L G X G A X L E E M K T> 13980 13930 13940 13950 13960 13970 13990 GCATGTCAGGGAGGGGAGGCCCTRGCCATAAGGCTAGAGTGTATTACAGAGACTCCAGGGACCCCMITTGGAAAGGCCC CGTACAGTCCCTCACCCTCCGGGAYCGGTATTCCGGTCTCACATAATGTCTCTGAGGTCCCTGGGGKAAACCTTTCCGGG A C Q G V G C P X H K A R V Y Y R D S R D P X W K G P> 14030 14050 14060 14070 14040 14080 pol 931-960 (96) TGCCAAACTGCTCTGGAAAGGCGAAGGCGCTGTGGTCATCCAAGAQRTTAAGATTGGAGGCCAACTGAHAGAAGCCCTCC ACGGTTGACGAGACCTTTCCGCTTCCGCGACACCAGTAGGTTCTGYAATTCTAACCTCCGGTTGACTWTCTTCGGGAGG
A K L L W K G E G A V V I Q D X K I G G Q L X E A L> 14150 14140 14090 14120 14130 pol 61-90 (38)  ${\tt TGGATACAGGAGCCGATGACACCGTCCTGGAAGAWATSANTCTGCCTGGCARGTGGGAATCAAACAGCTCCAGGCTAGGACCTATGTCCTCGGCTACTGTGGCAGGACCTTCTWTASTTAGACGGACCGTYCACCCTTAGTTTGTCGAGGTCCGATCC$ L D T G A D D T V L E X X N L P G X W G I K Q L Q A R> 14180 env 360-389 (160) 14210 14220 14170 GTCCTGGCTRTCGAGAGGTATCTGAAAGATCAANAGYTTCTGGGANTCTGGGGCTGTAGCGGAAAGGCTGCTATGGAAAA CAGGACCGAYAGCTCTCCATAGACTTTCTAGTTXTCRAAGACCCTKAGACCCGGACATCGCCTTTTCGGACGATACCTTTT V L A X E R Y L K D Q X X L G X W G C S G K A A 14260 14310 14250 vif 1-30 (100) CAGATGCCAACTCHTCATCGTCTGCCAACTCGACACGATCARGATTACGACATCGAAWAGCCTCGTGAAACACCATATGY GTCTACCGTTCACKACTAGCAGACCGTTCACCTGTCCTACTYCTAATCCTGTACCTTWTCGGAGCACTTTGTGGTATACR R W Q V X I V W Q V D R M X I R T W X S L V K H H M> 14330 14350 14360 env 390-419 (162) 14390 14340 A THITTATCTGTACCACARHCGTCCCCTGGAACTCCASCTGGAGCAATAAGTCCYTCGAAGAGATTTGGRATAACATGACC THANTAGACATGGTGTYRGCAGGGGACCTTGAGGTSGACCTCGTTATTCAGGRAGCTTCTCTAAACCYTATTGTACTGG XICTTXVPWNSXWSNKSXEEIWXNMT>

# FIGURE 15 (Cont)

14410 14420 14430 vpu 16-45 (133) 14460 14470 TGGATKSAATGGCTGATTHTCGCTATCGTCGTGTGGACCATTGYGTHTATCGAATACARGAAACTGCTCARGCAAAGGAR ACCTAMSTTACCGACTAAKAGCGATAGCAGCACACCTGGTAACRCAWATAGCTTATGTYCTTTGACGAGTYCGTTTCCTY W X X W L I X A I V V W T I X X I E Y X K L L X Q R X> 14490 14500 14510 14520 gag 46-75 (4) 14550 AATCGATAGGCTCATCRAAAGGCTCAACCCTGGCCTCCTGGAAACCKCTGAGGGATGTMAACAGATCCTGGRACAGCTCC TTAGCTATCCGAGTAGTTTTCCGAGTTCGGACCGGAGGACCTTTCGAGACCTACAKTTGTCTAGGACCYTGTCGAGG 14570 14580 14590 14600 14610 Q X A L X T G X E E L S S R K L L X Q R X I D R L I X> 14670 vpu 31-60 (134) 14680 14690 14700 14710 AGANYCAGAGAGAGAGCCGAAGACTCCGGCAATGAGTCCGAGGGAGAACACCCGGAATCAGATACCAATACAATGTGCT TCTTRGTCTCTCTCGGCTTCTGAGGCCGTTACTCAGGCTCCCTCTTGTGGGCCCTTAGTCTATGTTATCACGA
R X R E R A E D S G N E S E G D T P G I R Y Q Y N V L> 14730 pol 286-315 (53) 14760 14770 14780 CCCCCAAGGCTGGAAGGGCTCCCCASCCATTTTCCAAAGCTCCATGACCMAAATCCTCATGATGCAAAGGGGAAACTTTA GGGGGTTCCGACCTTCCCGAGGGGTSGGTAAAAGGTTTCGAGGTACKGGKTTTAGGAGTACTACGTTTCCCCTTTCAAAT PQGNKGSPXTPQSSNXXILNNQRGNF> 14820 14810 gag 376-405 (26) 14850 14860 rgggachgaaaaggathtcaagtgcttcaactgtggaaaggaaggccathtcgctargaattgcag/cctccctggag YCCCTGRCTTTTCCTAAYAGTTCACGAAGTTGACACCTTTCCTTCCGGTARAGCGATYCTTAACGTCTGGAGGGGACCTC
X G X K R I X K C P N C G K E G H X A X N C R P P L E> 14900 14890 14910 14940 rev 76-105 (129) AGACTGHACCTGGATTGCTCCGAGGATWGCGRCACCTCCGGCACACAGCAAAGCCAAGGCACAGAGACAGGAGTGGGA V C 14970 15000 pol 781-810 (86) 15030 15040 CGTGGCTGTGCXTGTGGCCAGCGGATATATCGAAGCCGAAGTGATCCCTGCCGAAACTGGACAGGAAACCGCTTACTTTM GCACCGACACGTACACCGGTCGCCTATATAGCTTCGGCTTCACTAGGGACGGCTTTGACCTGTCCTTTTGGCGAATGAAAK V A V H V A S G Y I E A E V I P A E T G Q E T A Y P> 15050 15060 15070 15080 15090 15120 env 200-229 (150) TCCTCANGATTARGCCTGTGGTCAGCACACAGCTCCTGCTCAACGGTAGCCTCGCTGAAGAGGAARTCRTTATCAGAAGC AGGAGTTQTXATYCGGACCAGTCGTGTGTGGGAGGACGAGTTGCCATCGGAGCGACTTCTCCTTYAGYAATAGTCTTCG X L K<sup>I</sup>I X P V V S 7 Q L L L N G S L A B B B X X I R S> 15130 15140 15150 15160 15170 pol 406-435 (61) GAAAACYTTACCRATAACAAACTGGTCGGCAAACTGAATTGGGCTTCCCAAATCTACSCTGGCATCAAAGTGARGCAACT CTTTTGRAATGGYTATTGTTGACCAGCCGTTTGACTTACCCCGAAGGGTTTACATCGACCGTAGTTCACTYCGTTGA
ENXTXNXLVGKLNWASQIYXGIXVXQL> 15230 15240 15250 env 121-139 (145) 15280 GTGTAAGCTCCTGAGAGGCRCCAAAGCCCTCACCCCTCTGTGTGACACTGAATTGCACAAACGCTAACCTCATCAATG spacers 15310 15320 15330 tat 76-102 (123) TGAN GCTGCICAANCCAGAGGCGATAACCCTACCGRTCCCRAAGAGTCCAAGAARAGGTCCAAGGTCCAAGRCAGAGACA
ACTTACGACGGTTKGGTCTCCGCTATTGGGATGGCYAGGGYTTCTCAGGTTCTTTYTCCAGCKCAGGTTCYGTCTCTGT U N A A Q X R G D N P T X P X E S K K X V X S K X E T>

FIGURE 15 (Cont)
SUBSTITUTE SHEET (RULE 26)

C4 join C5

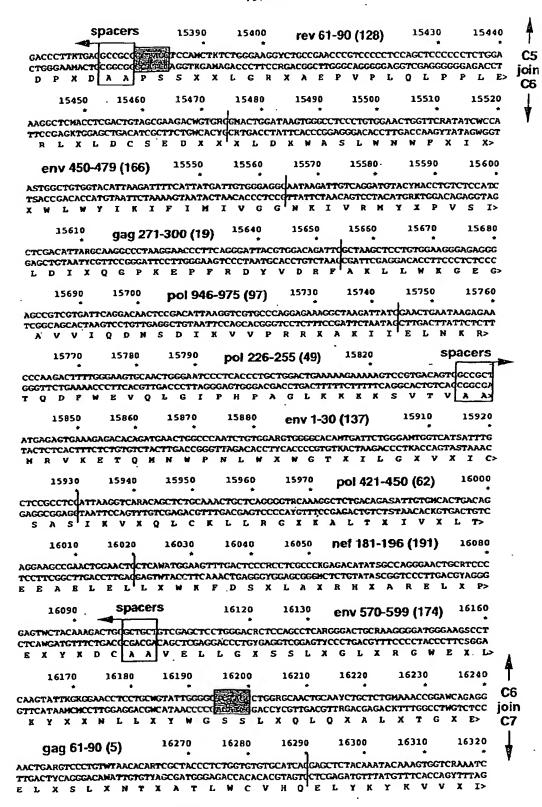


FIGURE 15 (Cont)

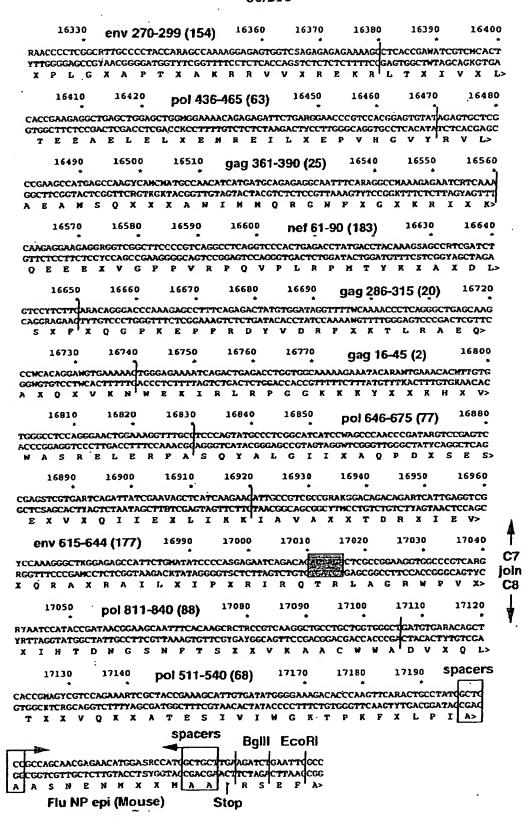


FIGURE 15 (Cont)

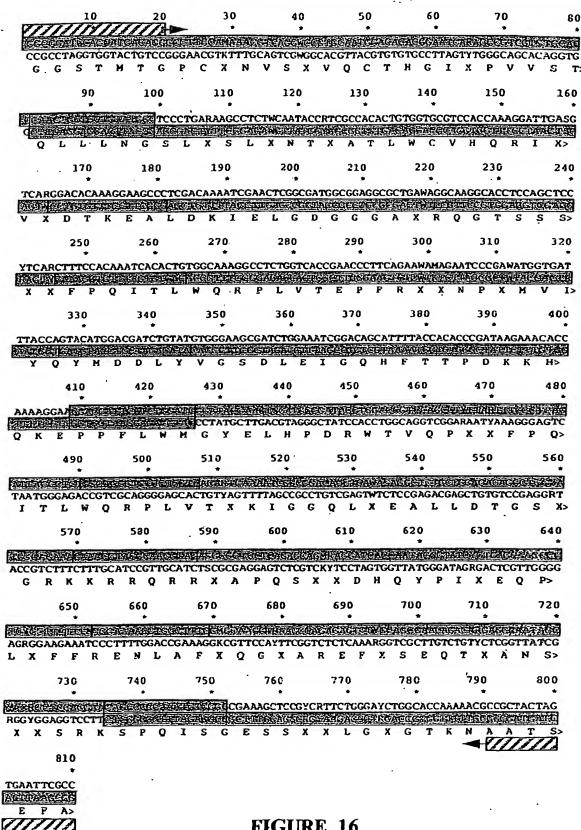


FIGURE 16

**SUBSTITUTE SHEET (RULE 26)** 

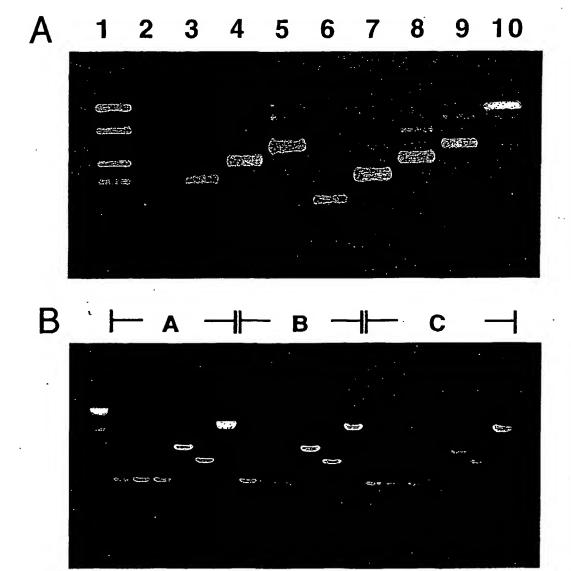


FIGURE 17

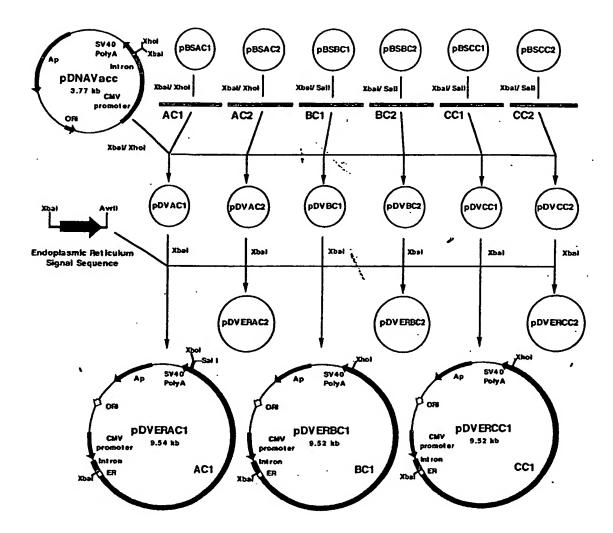


FIGURE 18A

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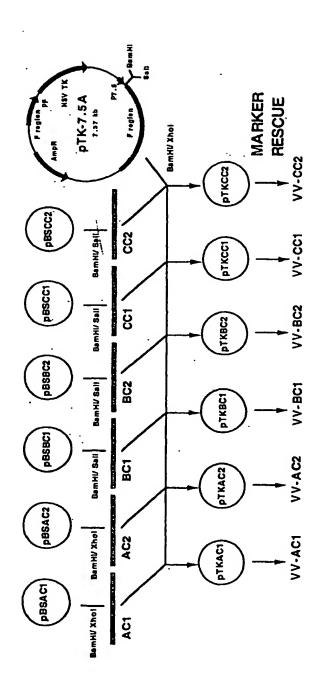


FIGURE 18B

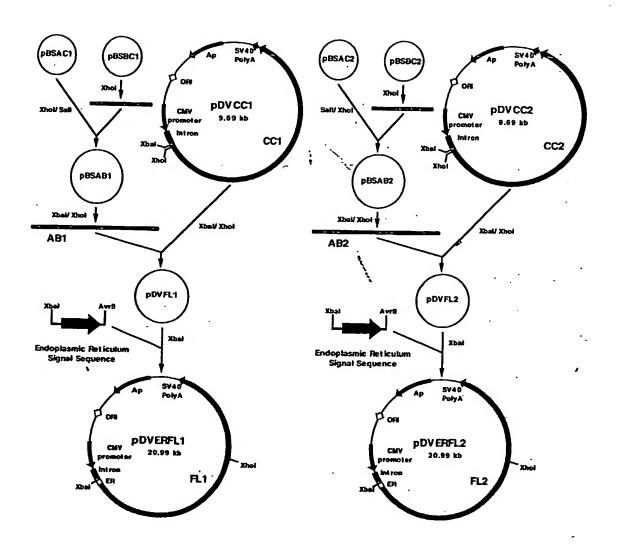
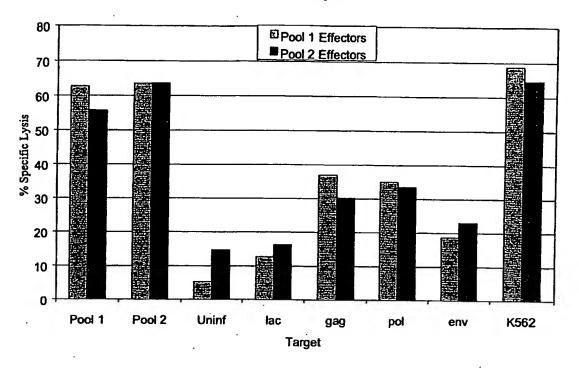


FIGURE 18C

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# Subject1





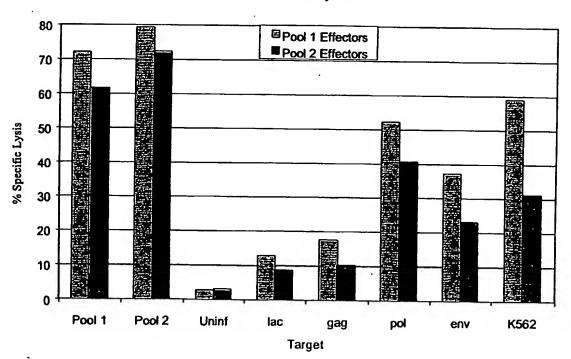


FIGURE 19

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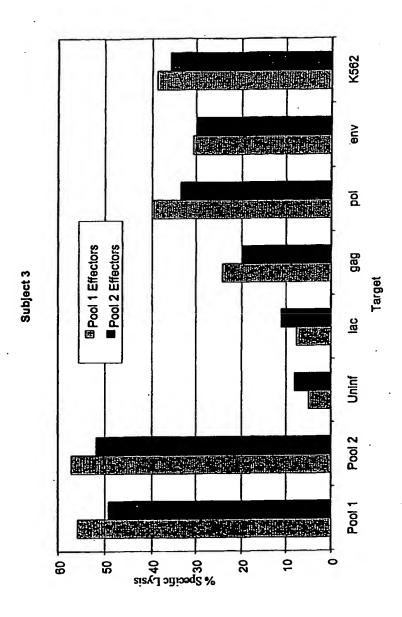


FIGURE 19 (Cont)

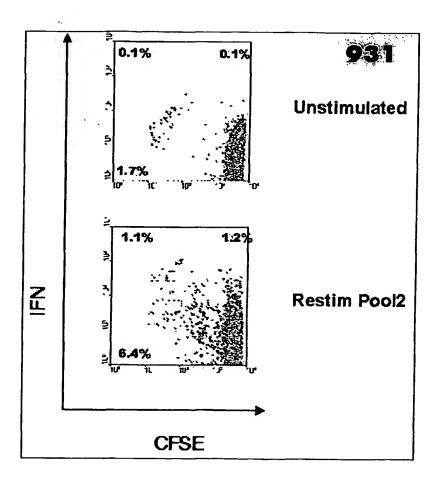


Figure 20

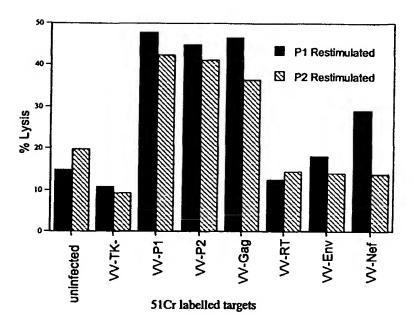


Figure 21

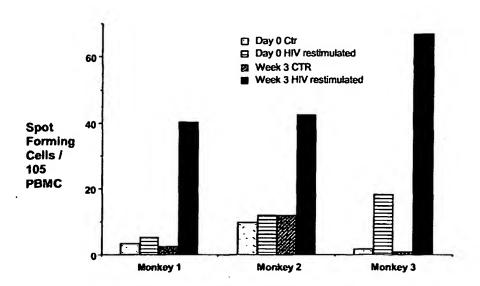


Figure 22A

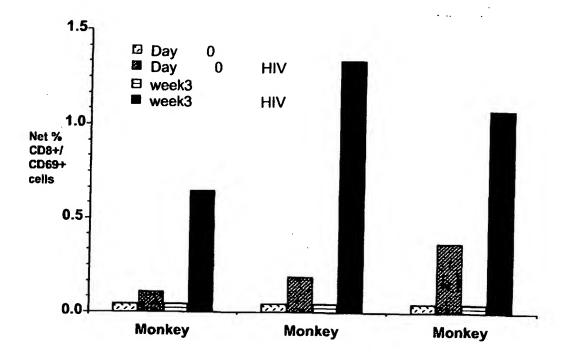


Figure 22B

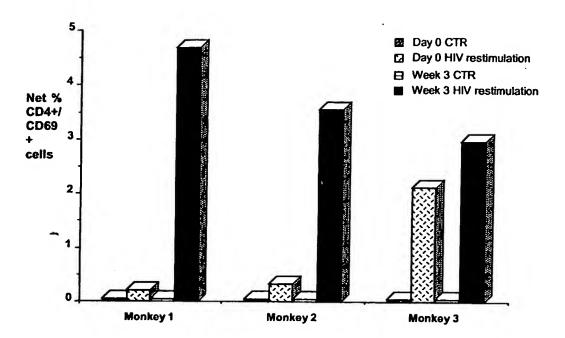


Figure 22C

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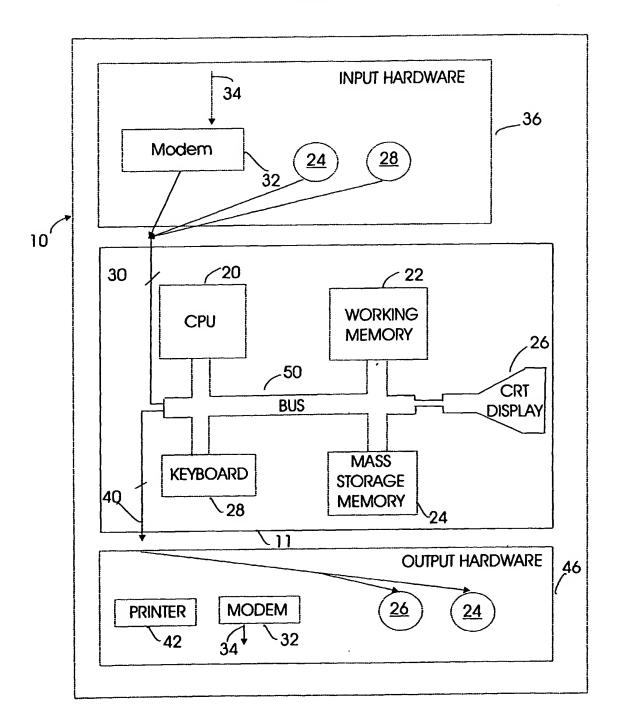


FIGURE 23

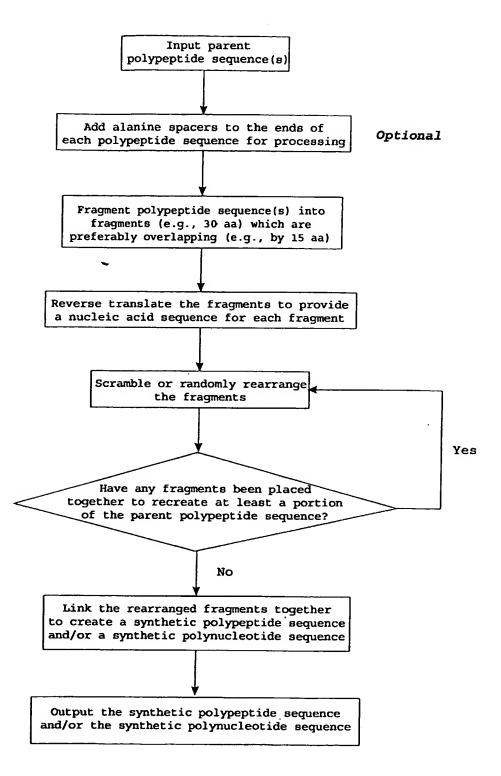


Figure 24

WO 01/090197

```
/* Scramble */
                                               95/216
 /* includes */
 #include <stdio.h>
 #include <stdlib.h>
 #include <string.h>
 #include <time.h>
 /* Constant definitions */
 /* Version Information */
 #define VERSION_NO
                                                                "0.2"
 #define VERSION_DATE
                                                     "04/03/1999"
 /* Misc */
 #define KEYBOARD_BUFFER_SIZE
                                           256
                                                               /*size of keyboard read buffer */
 #define LEN_CODON
                                                                         /*length of codon (including
 null) */
 #define BUFFER_SIZE
                                                               10000
                                                                         /*size of file read buffer */
 #define TRUE
                                                               1
                                                                                    /*boolean true */
 #define FALSE
                                                               0
                                                                                    /*boolean false */
 /* Error codes */
 #define E_NOERROR
                                                     0
                                                                         /*no error */
 #define E_NOINFILE
                                                     1
                                                                         /*genes file not found */
 #define E MALLOC
                                                    2
                                                                         /*memory allocation error */
 #define E FILEREAD
                                                    3
                                                                         /*file read error */
 #define E_CREATE OUTPUT FILE
                                                               /*error creating output file */
#define E_OVERLAP
                                                    5
                                                                         /*segment overlap >= length
/* Structure definitions */
typedef struct gene GENE;
typedef GENE * P_GENE;
typedef struct gene_segment GENE_SEGMENT;
typedef GENE_SEGMENT * P_GENE_SEGMENT;
struct gene {
          char * name;
          char * data;
          P_GENE next_gene;
};
int number;
          int offset;
          int first_codon_choice;
          char * amino_data;
          char * dna_data;
          P_GENE_SEGMENT next_seg;
}:
```

```
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  /* Function prototypes */
  int prolog();
  int get_parameters();
  int read_int(char * prompt);
  int load_genes();
 int add_gene(char * gene_name,char * gene_data);
 void insert_gene(P_GENE * head,P_GENE new_gene);
 int add aa();
 int split_genes();
 int split_gene(P_GENE g);
 int insert_segment(P_GENE_SEGMENT * head_seg,P_GENE_SEGMENT new_seg);
 int convert_segments_aa_to_dna();
 int convert_aa_to_dna(char * aa_ptr,char * dna_ptr,int first_choice);
 char * codon(char acid_char,int preferred);
 int perform scramble();
 int scramble_segments();
 int adjacent_segments();
 int display_genes();
 int write_output_file();
 void strip_newline(char * strip_str);
 void pad_amino_string(char * amino_ptr, char * padded_ptr);
 int even(int test_num);
 void read_str(char * prompt,char * string);
char * read_nonblank_line(char * buf,int buf_size,FILE * in_file);
 int user confirmation();
 void test();
 /* Global variables */
 char * codon_table[26][2] = {
/" A 00 "/ {"GCC","GCT"},
/" - 01 "/ {"???","???"},
/" C 02 "/ {"TGC","TGT"},
/" D 03 "/ {"GAC","GAT"},
/" E 04 "/ {"GAG", "GAA"},
 /" F 05 */ {"TTC","TTT"},
 /" G 06 "/ {"GGC", "GGA"},
/" H 07 "/ {"CAC","CAT"},
/" 1 08 "/ {"ATC","ATT"},
/" - 09 */ {"???","???"},
/" K 10 "/ {"AAG","AAA"},
/" L 11 "/ {"CTG","CTC"},
/" M 12 "/ {"ATG","ATG"},
/" N 13 "/ {"AAC","AAT"},
/" - 14 "/ {"???","???"),
/" P 15 "/ {"CCC","CCT"},
/" Q 16 "/ {"CAG","CAA"},
/" R 17 "/ {"AGG","AGA"},
/" S 18 */ {"AGC","TCC"},
/" T 19 "/ {"ACC","ACA"},
/* - 20 */ {**???*,"????"},
/" V 21 "/ {"GTG", "GTC"}
/" W 22 1/ ("TGG","TGG"),
```

Figure 25 (Cont)

```
/* - 23 */ {"???","???"},
 /" Y 24 "/ {"TAC", "TAT"},
                                                  97/216
/" - 25 */ {"???","????"}
};
char * error_text[] = {
/* 00 */ ···
/* 01 */ ,"ERROR: Input file not found!"
/* 02 */ ,"ERROR: Memory allocation error"
/* 03 */ ,"ERROR: File read error"
/* 04 */ ,"ERROR: Could not create output file"
/* 05 */ ,"ERROR: Segment overlap must be less than segment length"
char disease name[KEYBOARD BUFFER SIZE]:
char input_file_name[KEYBOARD_BUFFER_SIZE];
char output_file_name[KEYBOARD BUFFER SIZE];
int num_genes = 0;
int num_segments = 0;
int len_segment;
int segment overlap;
P_GENE first_gene = NULL;
P_GENE_SEGMENT first_segment = NULL;
P_GENE_SEGMENT * scrambled segments = NULL;
/* Mainline */
void main() {
           int error = E_NOERROR;
          printf("Scramble - Version %s, %s\n\n", VERSION_NO, VERSION_DATE);
           /* Initial processing */
          if (!error)
                     error = prolog();
          /* Get various program parameters from user */
          if (!error)
                     error = get_parameters();
          /* Load genes from genes file */
          if (!error)
                     error = load genes();
          /* Add 'AA' to start and end of all genes */
          if (!error)
                     error = add aa();
          /* Split genes into overlapping chunks */
          if (!error)
                     error = split_genes();
          /* Convert segment amino acid to dna */
          if (!error)
                     error = convert_segments_aa_to_dna();
```

Figure 25 (Cont)

```
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            /* Scramble the segments */
            if (!error)
                        error = perform_scramble();
            /* Write output file */
            if (!error)
                        error = write_output_file();
            /* Show error if there was one */
            if (error)
                       printf("%s\n",error_text[error]);
}
/* prolog() */
/* Perform any initial processing required */
int prolog() {
            /* Seed the random number generator, using the system clock */
            /* Don't run the program more than once in the same second! */
            /* Or we'll get the same randomisation!!!!!!!!!!!! */
            srand(time(NULL));
            return E_NOERROR;
}
/* get_parameters() */
/* Ask for various parameters from the user (stdin) */
     Disease name
[*
     Input file name
     Output file name
     Segment length
                                        */
int get_parameters() {
           int valid:
           read_str("Enter disease name : ",disease name);
           read_str("Enter input file name : ",input_file_name);
           read_str("Enter output file name : ",output_file_name);
           valid = FALSE;
           while (!valid) {
                      len_segment = read_int("Enter segment length : ");
                      if (len_segment % 2)
                                 printf("Segment length must be even!\n");
                      else
                                 valid = TRUE;
           segment_overlap = len_segment / 2;
           return E_NOERROR;
/* load genes() */
```

Figure 25 (Cont)

```
/* Load the genes from the input file */
                                                99/216
int load_genes() {
           FILE * input_file;
           char name_buf[BUFFER_SIZE];
           char data_buf[BUFFER_SIZE];
           /* Open genes file for reading */
           if (NULL == (input file = fopen(input_file_name, "r")))
                      return E NOINFILE;
           printf("Loading genes from: %s\n",input file name);
           num_genes = 0;
           /* Read gene name */
           while (NULL != read_nonblank_line(name_buf,BUFFER_SIZE,input_file)) {
                      /* Read the gene data */
                      if (NULL != read_nonblank_line(data_buf,BUFFER_SIZE,input_file)) {
                                 /* Allocate memory for new gene and add to list */
                                 if (rc = add_gene(name_buf,data_buf))
                                           break;
                     }
           /* Close genes file */
           fclose(input_file);
           return rc;
}
/* add gene() */
/* Allocate memory for new gene, then insert in list */
int add_gene(char * gene_name,char * gene_data) {
          P_GENE new_gene;
          /* Allocate storage for new gene */
          if (NULL == (new_gene = malloc(sizeof(GENE))))
                     return E_MALLOC;
          /* Initialise new gene */
          new gene->next gene = NULL;
          /* Allocate storage for gene name (+1 for null) */
          if (NULL == (new_gene->name = malloc(strlen(gene_name)+1)))
                     return E_MALLOC;
          /* Store gene name */
          strcpy(new_gene->name,gene_name);
          /* Allocate storage for gene data (+1 for null) */
          if (NULL == (new_gene->data = malloc(strlen(gene_data)+1)))
                     return E_MALLOC;
          /* Store gene data */
          strcpy(new gene->data,gene data);
          /* Insert the new gene into linked list */
          insert_gene(&first_gene,new_gene);
          /* Increment num_genes */
          num_genes++;
```

Figure 25 (Cont)

```
return E_NOERROR;
                                               100/216
}
/* insert_gene() */
/* Insert gene into linked list */
void insert_gene(P_GENE * head_gene,P_GENE new_gene) {
           P_GENE * cur_ptr = head_gene;
           while (NULL != (*cur_ptr))
                      cur_ptr = &((*cur_ptr)->next_gene);
           *cur_ptr = new_gene;
}
/* add_aa() */
/* Add 'AA' to the start and end of every gene */
char * new_data;
          while (NULL != cur_gene) {
                     /* Allocate storage to fit the gene plus four characters */
                     new_data = malloc(strlen(cur_gene->data)+5);
                     /* Shift gene data to new storage, add "AA" */
                     strcpy(new_data,"AA");
                     strcat(new_data,cur_gene->data);
                     strcat(new_data,"AA");
                     /* Free previous gene data storage */
                     free(cur gene->data);
                     /* Set gene data pointer to new storage */
                     cur_gene->data = new_data;
                     /* Advance to next gene */
                     cur_gene = cur_gene->next_gene;
          }
          return E_NOERROR;
/* split genes() */
/* Split the genes into overlapping segments */
int split_genes() {
          P_GENE cur_gene = first_gene;
          P_GENE_SEGMENT cur_seg = first_segment;
          printf("Splitting genes into segments...\n");
          /* Split the genes into segments */
          while (NULL != cur_gene) {
                    /* Split the gene */
                    split gene(cur gene);
                    /* Advance to next gene */
```

Figure 25 (Cont)

```
cur_gene = cur_gene->next gene;
           }
           /* Count the number of segments */
           num_segments = 0;
           cur_seg = first_segment;
           while (NULL != cur_seg) {
                     num segments++:
                      cur_seg = cur_seg->next_seg;
          }
          return E_NOERROR;
}
/* split_gene() */
/* Split a gene into overlapping segments */
int split_gene(P_GENE g) {
          char * seg_ptr;
          char * seg_buf;
          P_GENE_SEGMENT new segment = NULL;
          int done;
          int seg_ctr = 0;
          /* Allocate memory for segment buffer */
          if (NULL == (seg_buf = malloc(len_segment+1)))
                    return E_MALLOC;
          /* Insert a null at the end of the segment buffer, */
          /* so we can use it as a string */
          seg_buf[len_segment] = '\0';
          /* Set segment pointer to start of gene data */
          seg_ptr = g->data;
          done = FALSE;
          while (!(done)) {
                    /* So we know if we copied data */
                    seg_buf[0] = \0';
                    /* Copy a segment of gene data to the segment buffer */
                    memcpy(seg_buf,seg_ptr,len_segment);
                    /* If there was some gene data copied to the buffer */
                    if (NULL != seg_buf[0]) {
                              /* Allocate storage for a new segment */
                              if (NULL == (new_segment = malloc(sizeof(GENE_SEGMENT))))
                                         return E_MALLOC;
                              /* Increment segment counter */
                              seg_ctr++;
                              /* Setup the new segment */
                              new_segment->p_gene = g;
                              new_segment->number = seg_ctr;
                              new_segment->offset = seg_ptr - g->data + 1;
                              new_segment->next_seg = NULL;
```

Figure 25 (Cont)

```
if (NULL == (new_segment->amino_data = malloc(len_segment+1)))
                                          return E_MALLOC;
                                if (NULL == (new_segment->dna_data = malloc(len_segment*3+1)))
                                          return E_MALLOC;
                                new_segment->amino_data[0] = '\0';
                                new_segment->dna_data[0] = 10;
                                /* Copy segment data from buffer to new segment */
                                strcpy(new_segment->amino_data,seg_buf);
                                /* Insert new segment into chain from gene */
                                insert_segment(&first_segment,new_segment);
                    `}
                     /* If we didn't read a full segment, we are finished! */
                     if (strlen(seg_buf) < len_segment)
                                done = TRUE;
                     /* Otherwise, advance segment pointer to next segment in buffer */
                     else
                               seg_ptr = seg_ptr + len_segment - segment_overlap;
          }
}
/* insert_segment() */
/* Insert a segment node at the end of the list */
while (NULL != (*cur_ptr))
                     cur_ptr = &((*cur_ptr)->next_seg);
          *cur_ptr = new_seg;
}
/* convert segments as to dna */
/* Go thru segments, and for each, convert amino acids to dna */
int convert_segments_aa_to_dna() {
          P_ĞENE_SEGMENT cur_seg = first_segment;
          int first choice = 1;
          int alternate:
          printf("Converting to DNA...\n");
         /* Work out if we need to alternate the first codon choice or not */
         /* Don't need to do this anymore, since the segment length is
         /* forced to be even, and the overlap is half the length (odd). */
         /*alternate = ((even(len_segment) && even(segment_overlap))
                              || (!even(len_segment) && !even(segment_overlap)));*/
         alternate = FALSE;
         while (NULL != cur_seg) {
                    cur_seg->first_codon_choice = first_choice;
                    convert_aa_to_dna(cur_seg->amino_data,cur_seg->dna_data,
                                                                       cur_seg->first codon choice);
```

```
/* Address next segment */
                         cur_seg = cur_seg->next_seg;
                         /* If we are alternating, alternate the first codon choice */
                         /*if (alternate)
                                    if (1 == first choice)
                                                first_choice = 2;
                                     else
                                                first_choice = 1;*/
             }
             return E_NOERROR;
 }
 /* convert_aa_to_dna */
 /* Converts a string of amino acid to dna */
 /* NOTE: assumes that buffer at dna_ptr is large enough to hold dna!!! */
 int convert_aa_to_dna(char * aa_ptr,char * dna_ptr,int first_choice) {
             char * p codon;
             int cur_preferred = first_choice;
            while (10' != *aa_ptr) {
                        p_codon = codon(*aa ptr,cur preferred);
                        strcat(dna_ptr,p_codon);
                        /* If we didn't find a codon, log a warning */
                        if (0 == strcmp(p_codon,"???\0"))
printf("WARNING: no codon found for amino acid!\n");
                        /* Alternate current preferred codon */
                        if (1 == cur_preferred)
                                   cur_preferred = 2;
                        else
                                   cur_preferred = 1;
                       aa_ptr++;
           }
            return E_NOERROR;
/* codon */
/* Returns a pointer to a codon corresponding to the amino acid passed */
/* The codon pointer is to 3 characters, plus a terminating null */
char * codon(char acid_char,int preferred) {
           int codon_table_index;
           char * codon_ptr;
           /* Determine index into codon_table (table starts at 'A') */
           codon_table_index = acid_char - 'A';
           /* Set pointer to appropriate codon */
           codon_ptr = codon_table[codon_table_index][preferred-1];
```

```
return codon_ptr;
 }
 /* display genes() */
 /* Display the name and data for all genes */
 int display_genes() {
            P_GENE cur_gene = first_gene;
            while (NULL != cur_gene) {
                       printf("%s\n",cur_gene->name);
                       printf("%s\n",cur_gene->data);
                       cur_gene = cur_gene->next_gene;
           }
           return E_NOERROR;
 /* perform_scramble() */
/* Scramble the segments */
/* Check for adjacent segments. If there are, rescramble */
int perform_scramble() {
           int done = FALSE;
           int rc = E_NOERROR;
           while (TRUE) {
                      rc = scramble_segments();
                      if (E_NOERROR == rc)
                                 if (adjacent_segments()) {
                                            printf("Adjacent segments detected! Rescramble? (y/n) ");
                                            if (!user_confirmation()) {
                                                      printf("WARNING: Adjacent segments in output
file.\n");
                                                      break;
                                           }
                                else
                                           break;
                     else
                                break;
          }
          return rc;
/* scramble_segments() */
/* Randomly scramble the segments, putting pointers in scrambled_segments[] */
int scramble_segments() {
          P_GENE_SEGMENT cur_seg = first_segment;
          P_GENE_SEGMENT temp;
          printf("Scrambling segments...\n");
```

Figure 25 (Cont)

```
/* Allocate storage for array of segment pointers */
            if (NULL == (scrambled_segments = malloc(sizeof(P_GENE_SEGMENT)*num_segments)))
                       return E MALLOC;
            /* First, initialise scrambled_segments in same order as linked list */
            while (cur_seg != NULL) {
                       scrambled_segments[i] = cur_seg;
                       cur_seg = cur_seg->next_seg;
            }
            /* Now, randomly scramble the segments */
            for (i=0;i<num_segments;i++) {
                                   = rand() % num segments;
                                      = scrambled segments[i];
                       scrambled_segments[i] = scrambled_segments[j];
                       scrambled_segments[j] = temp;
           }
            return E NOERROR:
/* adjacent_segments() */
/* Determine if the scrambled segment order has resulted in */
/* two segments which were adjacent originally (ie every */
/* second one) have ended up adjacent.
int adjacent_segments() {
           int i:
           int rc = 0;
           P_GENE_SEGMENT cur_seg;
           P_GENE_SEGMENT next_seg;
           for (i=0;i<num segments-1;i++) {
                      /* Address current and next segments */
                      cur_seg = scrambled segments[i];
                      next_seg = scrambled_segments[i+1];
                      /* Do segments come from same gene, and are two apart? */
                      if (((cur_seg->p_gene == next_seg->p_gene)
                                && ((cur_seg->number == (next_seg->number)+2)
                                           || (cur_seg->number == (next_seg->number)-2))))
                                return 1:
           return 0;
}
/* write output_file() */
/* Write out segments (in initial non-scrambled order) */
/* Write out synthetic protein (in scrambled order) */
/* Write out synthetic dna (in scrambled order) */
int write_output_file() {
          FILE * output_file;
```

```
char * amino_buffer;
 P_GENE_SEGMENT cur_seg;
 /* Open output file for writing (erase any contents) */
 if (NULL == (output file = fopen(output_file_name, "w")))
             return E CREATE OUTPUT FILE;
 /* Allocate memory for padded amino string buffer */
 if (NULL == (amino_buffer = malloc(len_segment*3+1)))
             return E MALLOC;
 printf("Writing output file: %s\n",output file name);
/* Write output file header information */
fprintf(output_file,"Scramble %s - Output File\n", VERSION_NO);
fprintf(output_file,"\n");
fprintf(output_file, "Disease name : %s\n", disease_name);
fprintf(output file;"Input filename : %s\n",input file name);
fprintf(output_file,"Output filename: %s\n",output_file_name);
fprintf(output_file,"Number genes : %d\n",num_genes);
fprintf(output_file,"Number segments : %d\n",num_segments);
fprintf(output file, "Segment length: %d\n", len segment);
fprintf(output_file,"Segment overlap : %d\n",segment_overlap);
/* Write out segments in initial non-scrambled order */
fprintf(output_file,"\n");
fprintf(output_file,"Segments in original order:\n");
fprintf(output_file,"-
cur_seg = first_segment;
while (NULL != cur_seg) {
            /* Format amino data to line up with codons */
            pad_amino_string(cur_seg->amino_data,amino_buffer);
                                        : %s\n",cur_seg->p_gene->name);
            fprintf(output_file,"Gene
            fprintf(output_file,"Segment#: %d\n",cur_seg->number);
            fprintf(output_file,"Offset : %d\n",cur_seg->offset);
            fprintf(output_file, "1st Codon: %d\n",cur_seg->first_codon_choice); fprintf(output_file, "%s\n",amino_buffer); fprintf(output_file, "%s\n",cur_seg->dna_data);
            fprintf(output_file,"\n");
            cur_seg = cur_seg->next_seg;
/* Write out segment names in scrambled order */
fprintf(output_file, "Segments in scrambled order:\n");
fprintf(output_file,"-
for (i=0;i<num_segments;i++) {
           /* Format amino data to line up with codons */
           pad_amino_string(scrambled_segments[i]->amino_data,amino_buffer);
           /* Write segment details */
            fprintf(output_file,"%s #%d\n",scrambled_segments[i]->p_gene->name,
                       scrambled_segments[i]->number);
           fprintf(output_file,"%s\n",amino_buffer);
fprintf(output_file,"%s\n",scrambled_segments[i]->dna_data);
           fprintf(output_file,"\n");
```

}

```
/* Write synthetic protein in one long string */
             fprintf(output_file, "Synthetic Protein:\n");
             fprintf(output_file,"---
             for (i=0;i<num_segments;i++)
                        fprintf(output_file,"%s",scrambled_segments[i]->amino_data);
             fprintf(output file,"\n\n");
            /* Write synthetic dna in one long string */
            fprintf(output_file, "Synthetic DNA:\n");
            fprintf(output file,"---
            for (i=0;i<num_segments;i++)
                        fprintf(output_file, "%s", scrambled segments[i]->dna data);
            return E_NOERROR;
 }
 /* strip newline() */
 /* Replace the first newline character with a null */
 void strip_newline(char * strip_str) {
            char * newline_pos;
            /* Find the newline char */
            newline_pos = strchr(strip_str,\n');
            /* If we found one, replace it with a null */
            if (NULL != newline pos)
                        newline_pos[0] = \0';
}
/* pad_amino_string */
/* Copy amino chars from amino_ptr to padded_ptr, padding each */
/* side with a space. */
void pad_amino_string(char * amino_ptr, char * padded_ptr) {
           while ('\0' != *amino_ptr) {
                       *padded_ptr = ' ';
                       padded_ptr++;
                        *padded_ptr = *amino_ptr;
                       padded_ptr++;
                       *padded ptr = ' ';
                       padded ptr++;
                       amino_ptr++;
           }
           /* Stick a null at the end of the padded string */
           *padded ptr = 10;
}
/* even() */
/* True if test_num is even, otherwise false */
```

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```
int even(int test_num) {
             return !(test_num % 2);
 }
 /* read int() */
 /* Read an integer from stdin. Keep trying until valid int > 0 entered. */
 /* Return the integer read, or 0 if error reading from stdin. */
 int read_int(char * prompt) {
             char buffer[KEYBOARD BUFFER_SIZE];
             int value read;
            int valid = FALSE;
            while (!valid) {
                        printf("%s",prompt);
                        valid = TRUE;
                        fgets(buffer,KEYBOARD_BUFFER_SIZE,stdin);
                        if (1 != sscanf(buffer, "%d", &value_read))
                                 valid = FALSE;
                        if (valid && (value_read < 1))
                                   valid = FALSE;
                       if (!valid)
                                   printf("Positive integer value please!\n");
            return value_read;
}
/* read_str() */
/* Read a string from the user (stdin) */
/* Strip the newline from it */
void read_str(char * prompt,char * string) {
            char buffer[KEYBOARD BUFFER SIZE];
           printf(prompt);
           fgets(buffer,KEYBOARD_BUFFER_SIZE,stdin);
           sscanf(buffer, "%s", string);
}
/* read_nonblank_line() */
/* Read a line from file until we get a non-blank one */
char * read_nonblank_line(char * buf,int buf_size,FILE * in_file) {
           char * return_ptr;
           /* Read lines until we get a non-black one, or EOF */
                      return_ptr = fgets(buf,buf_size,in_file);
           while ((NULL != return_ptr) && (('\n' == buf[0]) || (' ' == buf[0])));
           /* If we got a line, change the newline char to a null */
           if (NULL != return ptr)
                      strip_newline(buf);
```

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```
return_ptr;
 }
 /* user_confirmation() */
 /* Read input from user. If user types 'y', return 1, otherwise 0 */
 int user_confirmation() {
              char buffer[KEYBOARD_BUFFER_SIZE];
              fgets(buffer,KEYBOARD_BUFFER_SIZE,stdin);
              if (('y' == buffer[0]) || ('Y' == buffer[0]))
                           return 1;
              else
                           return 0;
}
/* test() */
/* For debugging/development */
void test() {
              char str[100];
             printf("Enter something: ");
             fgets(str,100,stdin);
printf("line1\n");
printf("%s",str);
printf("line2\n");
fgets(str,100,stdin);
}
```

#### 110/216

HepC Savine design

# HepC la consensus polyprotein sequence used for scramble program

 ${\tt MSTNPKPQRKTKRNTNRRPQDVKFPGGGQIVGGVYLLPRRGPRLGVRATRKTSERSQPRGRRQPIPKARRPEGRTWAQ}$ PGYPWPLYGNEGCGWAGWLLSPRGSRPSWGPTDPRRRSRNLGKVIDTLTCGFADLMGYIPLVGAPLGGAARALAHGVR VLEDGVNYATGNLPGCSFSIFLLALLSCLTVPASAYQVRNSTGLYHVTNDCPNSSIVYEAADAILHTPGCVPCVREGN  ${\tt ASRCWVAMTPTVATRDGKLPATQLRRHIDLLVGSATLCSALYVGDLCGSVFLVGQLFTFSPRRHWTTQGCNCSIYPGH}$  ${\tt ITGHRMAWDMMMNWSPTAALVMAQLLRIPQAILDMIAGAHWGVLAGIAYFSMVGNWAKVLVVLLLFAGVDAETHVTGG}\\$  ${\tt NAGRTTSGLVSLLTPGAKQNIQLINTNGSWHINSTALNCNESLNTGWLAGLFYQHKFNSSGCPERLASCRRLTDFDQG}$ WGPISYANGSGPDQRPYCWHYPPKPCGIVPAKSVCGPVYCFTPSPVVVGTTDRSGAPTYSWGANDTDVFVLNNTRPPL GNWFGCTWMNSTGFTKVCGAPPCVIGGAGNNTLHCPTDCFRKHPEATYSRCGSGPWITPRCLVDYPYRLWHYPCTINY YGVGSSIASWAIKWEYVVLLFLLLADARVCSCLWMMLLISQAEAALENLVILNAASLAGTHGLVSFLVFFCFAWYLKG RWVPGAVYALYGMWPLLLLLLALPQRAYALDTEVAASCGGVVLVGLMALTLSPYYKRYISWCLWWLQYFLTRVEAQLH VWVPPLNVRGGRDAVILLMCVVHPTLVFDITKLLLAVFGPLWILQASLLKVPYFVRVQGLLRICALARKMIGGHYVQM AIIKLGALTGTYVYNHLTPLRDWAHNGLRDLAVAVEPVVFSQMETKLITWGADTAACGDIINGLPVSARRGREILLGP ADGMVSKGWRLLAPITAYAQQTRGLLGCIITSLTGRDKNQVEGEVQIVSTAAQTFLATCINGVCWTVYHGAGTRTIAS PKGPVIQMYTNVDQDLVGWPAPQGSRSLTPCTCGSSDLYLVTRHADVIPVRRRGDSRGSLLSPRPISYLKGSSGGPLL CPAGHAVGIFRAAVCTRGVAKAVDFIPVENLETTMRSPVFTDNSSPPAVPQSFQVAHLHAPTGSGKSTKVPAAYAAOG YKVLVLNPSVAATLGFGAYMSKAHGIDPNIRTGVRTITTGSPITYSTYGKFLADGGCSGGAYDIIICDECHSTDATSI LGIGTVLDQAETAGARLVVLATATPPGSVTVPHPNIEEVALSTTGEIPFYGKAIPLEVIKGGRHLIFCHSKKKCDELA  ${\tt AKLVALGINAVAYYRGLDVSVIPTSGDVVVVATDALMTGYTGDFDSVIDCNTCVTQTVDFSLDPTFTIETTTLPQDAV}$ SRTQRRGRTGRGKPGIYRFVAPGERPSGMFDSSVLCECYDAGCAWYELTPAETTVRLRAYMNTPGLPVCQDHLEFWEG VFTGLTHIDAHFLSQTKQSGENFPYLVAYQATVCARAQAPPPSWDQMWKCLIRLKPTLHGPTPLLYRLGAVQNEVTLT HPVTKYIMTCMSADLEVVTSTWVLVGGVLAALAAYCLSTGCVVIVGRIVLSGKPAIIPDREVLYREFDEMEECSQHLP YIEQGMMLAEQFKQKALGLLQTASRQAEVIAPAVQTNWQKLEVFWAKHMWNFISGIQYLAGLSTLPGNPAIASLMAFT AAVTSPLTTSQTLLFNILGGWVAAQLAAPGAATAFVGAGLAGAAIGSVGLGKVLVDILAGYGAGVAGALVAFKIMSGE VPSTEDLVNLLPAILSPGALVVGVVCAAILRRHVGPGEGAVQWMNRLIAFASRGNHVSPTHYVPESDAAARVTAILSS LTVTQLLRRLHQWISSECTTPCSGSWLRDIWDWICEVLSDFKTWLKAKLMPQLPGIPFVSCQRGYKGVWRGDGIMHTR CHCGAEITGHVKNGTMRIVGPRTCRNMWSGTFPINAYTTGPCTPLPAPNYTFALWRVSAEEYVBIRRVGDFHYVTGMT TONLKCPCQVPSPEPFTELDGVRLHRFAPPCKPLLREEVSFRVGLHEYPVGSQLPCEPEPDVAVLTSMLTDPSHITAE AAGRRLARGSPPSMASSSASQLSAPSLKATCTANHDSPDAELIEANLLWRQEMGGNITRVESENKVVILDSFDPLVAE EDBREISVPABILRKSRRFAQALPVWARPDYNPPLVETWKKPDYEPPVVHGCPLPPPRSPPVPPPRKKRTVVLTESTL STALAKLATKSPGSSSTSGITGDNTTTSSEPAPSGCPPDSDAESYSSMPPLEGEPGDPDLSDGSWSTVSSEAGTEDVV CCSMSYSWTGALVTPCAAEEQKLPINALSNSLLRHHNLVYSTTSRSACQRQKKVTFDRLQVLDSHYQDVLKEVKAAAS KVKANLLSVEEACSLTPPHSAKSKFGYGAKDVRCHARKAVAHINSVWKDLLEDSVTPIDTTIMAKNEVFCVQPEKGGR KPARLIVFPDLGVRVCBKMALYDVVSKLPLAVMGSSYGFQYSPGQRVEFLVQAWKSKKTPMGFSYDTRCFDSTVTESD IRTEEAIYQCCDLDPQARVAIKSLTERLYVGGPLTNSRGENCGYRRCRASGVLTTSCGNTLTCYIKARAACRAAGLQD CTMLVCGDDLVVICESAGVQEDAASLRAFTEAMTRYSAPPGDPPQPEYDLELITSCSSNVSVAHDGAGKRVYYLTRDP TTPLARAAWETARHTPVNSWLGNIIMFAPTLWARMILMTHPFSVLIARDQLEQALDCEIYGACYSIEPLDLPPIIQRL HGLSAFSLHSYSPGEINRVAACLRKLGVPPLRAWRHRARSVRARLLARGGRAAICGKYLFNWAVRTKLKLTPIAAAGR LDLSGWFTAGYSGGDIYHSVSHARPRWFWFCLLLLAAGVGIYLLPNR

```
Scramble - Output Pile
Scramble version: 0.1 beta, 08/02/1999
              : 1
Num. genes
Num. segments
               : 201
Segment length
               : 30
Segment overlap : 15
Segments in original order:
Gene
        : HepCla
Segment#
        : 1
Offset
       : 1
1st Codon : 1
A A M S T N P K P Q R K T K R N T N R R P Q D V K P P G G G
GCCGCTATGTCCACCAATCCCAAACCCCAAAGGAAAACCAAAAGGAATACCAATAGGAGACCCCAAGACGTCAAGTTTCCCGGAGGCGGA
```

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Gene : HepCla Segment# : 2 Offset : 16 1st Codon : 1

N T N R R P Q D V K P P G G G Q I V G G V Y L L P R R G P R AACACAAACAGAAGGCCTCAGGATGTGAAATTCCCTGGGGGGGCCAAATCGTCGGCGGAGTGTATCTGCTCCCCAGAAGGGGACCCAGA

Gene : HepCla Segment# : 3 Offset : 31 1st Codon : 1

Q I V G G V Y L L P R R G P R L G V R A T R K T S E R S Q P CAGATTGTGGGAGGCGTCTACCTCCTGCCTAGGAGGGCCCCTAGGCTCAGGGCTACCAGAAAGACAAGCGAAAGGTCCCAGCCT

Gene : HepCla
Segment# : 4
Offset : 46
1st Codon : 1

L G V R A T R K T S E R S Q P R G R R Q P I P K A R R P E G CTGGGAGTGAGGCCCACACGAAGGCCACCCAGAGGCCAAAGCCCAAAGCCAGAAGGCCTGAGGGA

Gene : HepCla Segment# : 5 Offset : 61 lst Codon : 1

Gene : HepCla
Segment# : 6
Offset : 76
lst Codon : 1

RTWAQPGYPWPLYGNEGCGNAGWLLSPRGSAGGAAAGGAAGGCTGGGCCGGATGGCTCCTGTCCCCAGAGGCTCC

Gene : HepCla Segment# : 7 Offset : 91 lst Codon : 1

EGCGWAGWLLSPRGSRPSWGPTDPRRRSRN GAGGGATGGGGTGGCTGGCTGGCCCTAGGGGAGCAGACCCTCCTGGGGACCCACAGACCCTAGGAGAAGGTCCAGGAAT

Gene : HepCla
Segment# : 8
Offset : 106
1st Codon : 1

R P S W G P T D P R R R S R N L G K V I D T L T C G F A D L AGGCCTAGCTGGGCCCCTACCGGAAGGAGGAGGAGAAGCTGGCAAACTGATTGACACACTGACATGCGGATTCGCTGACCTC

Gene : HepCla Segment# : 9 Offset : 121 1st Codon : 1

L G K V I D T L T C G P A D L M G Y I P L V G A P L G G A A CTGGGAAGGTCATCGATGCCTCTGGCCTTGGCCTTTGCCGATCTGATGCGCTATATCCCTCTGGTCGGCGGCCGCTCCCCTCGGCGGAGCCGCT

Gene : HepCla Segment# : 10 Offset : 136 1st Codon : 1

M G Y I P L V G A P L G G A A R A L A H G V R V L B D G V N ATGGGATACATTCCCTCGTGGGAGGCCCTCTGGGAGGCCCTCGCCAGGCCCTCGCCCATGGCGTCAGGGTCATGAAT

Gene : HepCla Segment# : 11 Offset : 151 1st Codon : 1

RALAHGVRVLBDGVNYATGNLPGCSPSIPL AGGGCTCTGGCTCACGGAGTGCTCGAGGATGGCCTCAACTATGCCACGGCAATCTGCCTGGCTGTAGCTTTAGCATTTTCCTC

Gene : HepCla Segment# : 12 Offset : 166

# 112/216

1st Codon : 1 Y A T G N L P G C S F S I F L L A L L S C L T V P A S A Y Q TACGCTACCGGAAACCTCCCCGGATGCTCCTTCTCCATCTTTCTGCTCGCCCTCCTGTCCTGCCTCACCGTCCCCGCTAGCGCTTACCAA : HepCla Segment# : 13 Offset : 181 1st Codon : 1 L A L L S C L T V P A S A Y Q V R N S T G L Y H V T N D C P CTGGCTCTGCTCAGCTGTCTGACAGTGCCTGCCTCCGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAAACGATTGCCCT Gene : HepCla Segment# : 14 Offset : 196 V R N S T G L Y H V T N D C P N S S I V Y E A A D A I L H T GTGAGAAACTCCACCGGACTGTATCACGTCACCAATGACTGTCCCAATAGCTCCATCGTCTACGAAGCCGCTGACGCTATCCTCCACACA Gene : HepCla Segment# : 15 : 211 Offset 1st Codon : 1 N S S I V Y E A A D A I L H T P G C V P C V R E G N A S R C AACTCCAGCATTGTGTATGAGGCTGCCGATGCCATTCTGCATACCCCTGGCTGTGTGCCTTGCGTCAGGGAAGGCAATGCCTCCAGGTGT Gene : HepCla Segment# : 16 Offset : 226 1st Codon : 1 PGCVPCVRBGNASRCWVAMTPTVATRDGKL CCCGGATGCGTCCCCTGTGTGAGAGAGGGAAACGCTAGCAGATGCTGGGTGGCTATGACACCCACAGTGGCTACCAGAGACGGAAAGCTC Gene : HepCla Segment# : 17 Offset : 241 1st Codon : 1 W V A M T P T V A T R D G K L P A T Q L R R H I D L L V G S Gene : HepCla Segment# : 18 Offset : 256 PATQLRRHIDLLVGSATLCSALYVGD LCGS CCCGCTACCCAACTGAGAAGGCATATCGATCTGCTCGTGGGAAGCGCTACCCTCTGCTCCGCCCTCTACGTCGGCGATCTGTGTGGCTCC Gene : HepCla Segment# : 19 : 271 Offset 1st Codon : 1 A T L C S A L Y V G D L C G S V F L V G Q L F T F S P R R H GCCACACTGTGTAGCGCTCTGTATGTGGGAGACCTCTGCGGAAGCGTCTTCCTCGTGGGACAGCTCTTCACATTCTCCCCCAGAAGGCAT Gene : HepCla Segment# : 20 Offset : 286 V F L V G Q L F T F S P R R H W T T Q G C N C S I Y P G H I GTGTTTCTGGTCGGCCAACTGTTTACCTTTAGCCCTAGGAGACACTGGACCACACGGGATGCAATTGCTCCATCTATCCCGGACACATT Gene : HepCla Segment# : 21 : 301 Offset 1st Codon : 1 N T T Q G C N C S I Y P G H I T G H R M A W D M M M N W S P TGGACAACCCAAGGCTGTAACTGTAGCATTTACCCTGGCCATATCACAGGCCCATAGGATGGCCCTGGGGACATGATGAACTGGAGCCCCT Gene : HepCla Segment# : 22 : 316 1st Codon : 1 T G H R N A N D M M N N S P T A A L V N A Q L L R I P Q A ACCGGACACAGAATGGCTTGGGATATGATGAATGGTCCCCCACAGCCGCTCTGGTCATGGCTCAGCTCCTGAGAATCCCTCAGGCT

## 113/216

: HepCla Segment# : 23 Offset : 331 1st Codon: 1 TAALVMAQLLRIPQAILDMIAGAHWGVLAG ACCECTECTCGTGATESCCCAACTECTCASGATTCCCCAAGCCATTCTGGATATGATTSCCGGAGCCCATTGGGGAGTGCTCGCCGGA Gene : HepCla Segment# : 24 Offset : 346 1st Codon : 1 I L D M I A G A H W G V L A G I A Y P S M V G N W A K V L V Gene : HepCla Segment# : 25 Offset : 361 1st Codon : 1 I A Y P S M V G N W A K V L V V L L L P A G V D A E T H V T ATCGCTTACTTTAGCATGGTGGGAAACTGGCCAAAGTGCTCGTGGTCCTGCTTCTGTTTGCCGGAGTGGATGCCGAAACCCATGTGACA Gene : HepCla Segment# : 26 : 376 Offset 1st Codon : 1 V L L F A G V D A E T H V T G G N A G R T T S G L V S L L GTGCTCCTGCTCTTCGCTGGCGTCGACGCTGAGACACACGTCACCGGAGGCAATGCCGGAAGGACAACCTCCGGCCTCGTGTCCCTGCTC Gene : HepCla Segment# : 27 Offset : 391 1st Codon : 1 G G N A G R T T S G L V S L L T P G A K Q N I Q L I N T N G GGCGGAAACGCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCCGGAGCCAAACAGAATATCCAACTGATTAACACAAACGGA Gene : HepCla Segment# : 28 Offset : 406 1st Codon : 1 T P G A K Q N I Q L I N T N G S W H I N S T A L N C N E S L ACCCCTGGCGCTAAGCAAAACATTCAGCTCATCAATACCCAATGGCTCCTGGCATATCAATAGCACAGCCCTCAACTGTAACGAAAGCCTC Gene : HepCla Segment# : 29 Offset : 421 1st Codon : 1 S W H I N S T A L N C N E S L N T G W L A G L F Y Q H K F N AGCTGGCACATTAACTCCACCGCTCTGAATTGCAATGAGTCCCTGAATACCGGATGGCTCGCCGGACTGTTTTACCAACACACAAATTCAAT Gene : HepCla Segment# : 30 Offset : 436 1st Codon : 1 N T G W L A G L P Y Q H K P N S S G C P B R L A S C R R L T AACACAGGCTGGCTGGCTGGCCTCTTCTATCAGCATAAGTTTAACTCCAGCGGATGCCCTGAGAGACTGGCTAGCTGTAGGAGACTGACA Gene : HepCla Segment# : 31 Offset : 451 1st Codon : 1 S S G C P B R L A S C R R L T D P D Q G W G P I S Y A N G S AGCTCCGGCTGTCCCGAAAGGCTCGCCTCCTGCAGAAGGCTCACCGATTTCGATCAGGGATGGGGACCCATTAGCTATGCCAATGGCTCC : HepCla Gene Segment# : 32 : 466 Offset D P D Q G W G P I S Y A N G S G P D Q R P Y C W H Y P P K P GACTTTGACCAAGGCTGGGGCCCTATCTCCTACGCTAACGGAAGCGGACCCGATCAGAGACCCTATTGCTGGCACTATCCCCCTAAGCCT Gene : HepCla Segment# : 33

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Offset : 481 1st Codon : 1 G P D Q R P Y C W H Y P P K P C G I V P A K S V C G P V Y C Gene : HepCla Segment# : 34 Offset : 496 1st Codon : 1 C G I V P A K S V C G P V Y C F T P S P V V G T T D R S G Gene : HepCla Segment# : 35 Offset : 511 1st Codon : 1 PTPSPVVGTTDRSGAPTYSWGANDTDVPV TTCACACCCTCCCCGTCGTCGCCACAACCGATAGGTCCGGCGCTCCCACATACTCCTCGGGGAGCCAATGACACGACGTCTTCGTC : HepCla Gene Segment# : 36 : 526 1st Codon : 1 A P T Y S W G A N D T D V P V L N N T R P P L G N W F G C T GCCCCTACCTATAGCTGGGGCGCTAACGATACCGATGTGTTTTGTGCTCAACAATACCAGACCCCCTCTGGGAAACTGGTTCGGATGCACA Gene : HepCla Segment# : 37 : 541 1st Codon : 1 LNNTRPPLGNWFGCTWMNSTGPTKVCGAPP  $\tt CTGAATAACACAAGGCCTCCCCTCGGCAATTGGTTTGGCTGTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCT$ Gene : HepCla Segment# : 38 Offset : 556 1st Codon : 1 W M N S T G P T K V C G A P P C V I G G A G N N T L H C P T Gene : HepCla Segment# : 39 Offset : 571 1st Codon : 1 CVIGGAGNNTLHCPTDCFRKHPBATYSRCG TGCGTCATCGGAGGCGCTGGCAATAACACACTGCATTGCCCTACCGATTGCTTTAGGAAACACCCTGAGGCTACCTATAGCAGATGCGGA Gene : HepCla Segment# : 40 Offset 1st Codon : 1 DCFRKHPBATYSRCGSGPWITPRCLVDYPY GACTGTTTCAGAAAGCATCCCGAAGCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTGGTCGACTATCCCTAT Gene : HepCla Segment# : 41 1st Codon : 1 SGPWITPRCLVDYPYRLWHYPCTINYTIPK AGCGGACCCTGGATCACACCCAGATGCCTCGTGGATTACCCTTACAGACTGTGGCACTATCCCTGTACCATTAACTATACCATTTTCAAA Gene : HepCla Segment# : 42 Offset : 616 1st Codon : 1 RL W H Y P C T I N Y T I P K V R M Y V G G V E H R L E A A AGGCTCTGGCATTACCCTTGCACAATCAATTACACAATCTTTAAGGTCAGGATGTACGTCGGCGGAGTGGAACACAGACTGGAAGCCGCT : HepCla Segment# : 43 Offset : 631 1st Codon : 1 V R M Y V G G V B H R L B A A C N W T R G E R C D L B D R D

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GTGAGAATGTATGTGGGAGCGTCGAGCATAGGCTCGAGGCTGCCTGTAACTGGACCAGAGGCGAAAGGTGTGACCTCGAGGATAGGGAT
 Gene
         : HepCla
        : 44
 Segment#
 Offset
 1st Codon : 1
 C N W T R G E R C D L E D R D R S E L S P L L S T T Q W Q
 TGCAATTGGACAAGGGGAGAGAGATGCGATCTGGAAGACAGAAGACAGAAGCGAACTGTCCCCCTCCTGCTCAGCACAACCCAATGGCAA
         : HepCla
Gene
Segment# : 45
Offset
         : 661
1st Codon : 1
 R S E L S P L L S T T Q W Q V L P C S F T T L P A L S T G
AGGTCCGAGCTCAGCCCTCTGCTCCTGTCCACCACACAGTGGCAGGTCCTGCCTTGCTCCTTCACAACCCTCCCCGGCTCTGTCCACCGGA
Gene
         : HepCla
Segment# : 46
Offset
        : 676
1st Codon : 1
 V L P C S F T T L P A L S T G L I H L H Q N I V D V Q Y L Y
: HepCla
Gene
Segment# : 47
Offset
        : 691
1st Codon : 1
 LIHLHQNIVDVQYLYGVGSSIASWAIKW<sub>BY</sub>
CTGATTCACCTCCACCAAAACATTGTGGATGTGCAATACCTCTACGGAGTGGGAAGCTCCATCGCTAGCTGGGCCATTAAGTGGGAGTAT
Gene
         : HepCla
Segment# : 48
Offset
        : 706
1st Codon : 1
 G V G S S I A S W A I K<sub>1</sub> W E Y V V L L F L L A D A R V C S
GGCGTCGGCTCCAGCATTGCCTCCTGGGCTATCAAATGGGAATACGTCGTGCTCCTGTTTCTGCTCCTGGCTGACGCTAGGGTCTGCTCC
Gene
        : HepCla
Segment# : 49
        : 721
Offset
1st Codon : 1
 V V L L P L L A D A R V C S C L W M M L L I S Q A E A A L
GTGGTCCTGCTCTCCTGCTGGCGATGCCAGAGTGTTAGCTGTTGTGGATGATGCTCCTCATCTCCAGGCTGAGGCTGAGGCTGCCCTC
        : HepCla
Gene
Segment# : 50
Offset
        : 736
1st Codon : 1
C L W M M L L I S Q A E A A L E N L V I L N A A S L A G T H
TGCCTCTGGATGATGCTCCTGATTAGCCAAGCCGAAGCCGCTCTGGAAAACCTCGTGATTCTGAATGCCGCTAGCCTCGCCGGAACCCAT
        : HepCla
Segment# : 51
Offset
        : 751
1st Codon : 1
B N L V I L N A A S L A G T H G L V S P L V F F C P A W Y L
GAGAATCTGGTCATCCTCAACGCTGCCTCCCTGGCTGCCACACGCGACTGGTCAGCTTTCTGGTCTTCTTTTGCTTTGCCTTGGTCACCTC
Gene
        : HepCla
Segment# : 52
Offset
        : 766
1st Codon : 1
G L V S P L V P P C P A W Y L K G R W V P G A V Y A L Y G M
GGCCTCGTGTCCTCCTCGTGTTTTCTGTTTCGCTTGGTATCTGAAAGGCAGATGGGTCCCCGGAGCCGTCTACGCTCTGTATGGCATG
Gene
        : HepCla
Segment# : 53
Offset
        : 781
1st Codon : 1
K G R W V P G A V Y A L Y G M W P L L L L L A L P Q R A Y
AAGGGAAGGTGGGTGCCTGGCGCTGTGTGTGCCCCTCTACGGAATGTGGCCCCTCCTGCTCCTGCTCCTGCCTCAGAGAGCCCTAT
Gene
        : HepCla
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Segment# : 54 Offset : 796 1st Codon : 1 W P L L L L L A L P Q R A Y A L D T E V A A S C G G V V L Gene : HepCla Segment# : 55 1st Codon : 1 ALDTEVAASCGGVVLVGLMALTLSPYYKRY GCCCTCGACACAGAGGTCGCCGCTAGCTGTGGCGGAGTGGTCCTGGTCGGCCTCATGGCTCTGACACTGTCCCCCTATTACAAAAGGTAT : HepCla Segment# : 56 Offset : 826 1st Codon : 1 V G L M A L T L S P Y Y K R Y I S W C L N W L Q Y F L T R V GTGGGACTGATGGCCCTCACCCTCAGCCCTTACTATAAGAGATACATTAGCTGGTGCCTCTGGTGGCTGCAATACTTTCTGACAAGGGTC : HepCla Segment# : 57 Offset : 841 1st Codon : 1 ISWCLWWLQYFLTRVEAQLHVWVPPLNVRG ATCTCCTGGTGTCTGTGGTGGCTCCAGTATTTCCTCACCAGAGTGGAAGCCCAACTGCATGTGTGGGTGCCTCCCCTCAACGTCAGGGGA Gene : HepCla Segment# : 58 Offset : 856 1st Codon : 1 E A Q L H V W V P P L N V R G G R D A V I L L M C V V H P T GAGGCTCAGCTCCACGTCTGGGTCCCCCCTCTGAATGTGAGAGGCGGAAGGGATGCCGTCATCCTCCTGATGTGCGTCGTGCATCCCACA : HepCla Segment# : 59 Offset : 871 1st Codon : 1 G R D A V I L L M C V V H P T L V F D I T K L L A V F G P GGCAGAGACGCTGTGATATCTGCTCATGTGTGTGGTCCACCCTACCCTCGTGTTTGACATTACCAAACTGCTCCTGGCTGTGTTTGGCCCCT Gene : HepCla Segment# : 60 : 886 Offset 1st Codon : 1 L V F D I T K L L L A V F G P L W I L Q A S L L K V P Y F V CTGGTCTTCGATATCACAAAGCTCCTGCTCGCCGTCTTCGGACCCCTCTTGGATTCTGCAAGCCTCCCTGCTCAAGGTCCCCTATTTCGTC Gene : HepCla Segment# : 61 Offset : 901 1st Codon : 1 LWILQASLLKVPYPVRVQGLLRICALARKM CTGTGGATCCTCCAGGCTAGCCTCCTGAAAGTGCCTTACTTTGTGAGAGTGCAAGGCCTCCTGAGAATCTGTGCCCTCGCCAGAAAGATG Gene : HepCla Segment# : 62 Offset : 916 1st Codon : 1 R V Q G L L R I C A L A R K M I G G H Y V Q M A I I K L G A AGGGTCCAGGGACTGCTCAGGATTTGCGCTCTGGCTAGGAAAATGATTGGCCGGACACTATGTGCAAATGGCTATCATTAAGCTCGGCGCT Gene : HepCla Segment# : 63 Offset : 931 1st Codon : 1 I G G H Y V Q M A I I K L G A L T G T Y V Y N H L T P L R D ATCGGAGGCCATTACGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACCGGAACCTATGTGTATAACCATCTGACACCCCTCAGGGAT Gene : HepCla Segment# : 64 Offset : 946 1st Codon : 1

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LTGTYVYN H LTPLR DWAHNGLR DLAVAVE P : HepCla Gene Segment# : 65 Offset : 961 1st Codon : 1 WAHNGLRDLAVAVEPVVFSQMETKLITWGA TGGGCTCACAATGGCCTCAGGGATCTGGCTGTGGCTGTGGAACCCGTCGTCTTTAGCCAAATGGAAACCAAACTGATTACCTGGGGCGCT : HepCla Gene Segment# : 66 Offset : 976 1st Codon : 1 V V P S Q M B T K L I T W G A D T A A C G D I I N G L P V S GTGGTCTTCTCCCAGATGGAGACAAAGCTCATCACATGGGGAGCCGATACCGCTGCCTGTGGCGATATCATTAACGGACTGCCTGTGTCC : HepCla Gene Segment# : 67 Offset : 991 1st Codon : 1 D T A A C G D I I N G L P V S A R R G R E I L L G P A D G M Gene : HepCla Segment# : 68 Offset : 1006 1st Codon : 1 ARRGREILLGPADGMVSKGWRLLAPITAYA GCCAGAAGGGGAAGGGAAATCCTCCTGGGACCCGCTGACGGAATGGTCAGCAAAGGCTGGAGGCTCCTGGCTCCCATTACCGCTTACGCT : HepCla Segment# : 69 Offset : 1021 1st Codon : 1 V S K G W R L L A P I T A Y A Q Q T R G L L G C I I T S L T GTGTCCAAGGGATGGAGACTGCTCGCCCCTATCACAGCCTATGCCCAACAGACAAGGGGACTGCTCGGCTGTATCATTACCTCCCTGACA : HepCla Segment# : 70 Offset : 1036 1st Codon : 1 Q Q T R G L L G C I I T S L T G R D K N Q V E G E V Q I V S CAGCAAACCAGAGGCCTCCTGGGATGCATTATCACAAGCCTCACCGGAAGGGATAAGAATCAGGTCGAGGGAGAGGGTCCAGATTGTGTCC : HepCla Gene Segment# : 71 Offset : 1051 1st Codon : 1 G R D K N Q V E G E V Q I V S T A A Q T P L A T C I N G V C GGCAGAGACAAAAACCAAGTGGAAGGCGAAGTGCAAATCGTCAGCACACGCCGCTCAGACATTCCTCGCCACATGCATTAACGGAGTGTG Gene : HepCla Segment# : 72 Offset : 1066 1st Codon : 1 TAAQTFLATCING V C W T V Y H G A G T R T I A S P ACCICTICCCAAACCTTTCTGGCTACCTGTATCAATGGCGTCTGCTGGACCGTCTACCATGGCGCTAGGCACAAGGACAATCGCTAGCCCT Gene : HepCla Segment# : 73 Offset : 1081 1st Codon : 1 W T V Y H G A G T R T I A S P K G P V I Q M Y T N V D Q D L TGGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCCAAAGGCCCTGTGATTCAGATGTACACAAACGTCGACCAAGACCTC Gene : HepCla Segment# : 74 Offset : 1096 1st Codon : 1 K G P V I Q M Y T N V D Q D L V G W P A P Q G S R S L T P C AAGGGACCCGTCATCCAAATGTATACCAATGTGGATCAGGATCTGGTCGGCTGGCCCGCTCCCCAAGGCTCCCAGGTCCCTGACACCCTGT

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Gene : HepCla Segment# : 75 Offset : 1111 1st Codon : 1

Gene : HepCla Segment# : 76 Offset : 1126 1st Codon : 1

T C G S S D L Y L V T R H A D V I P V R R R G D S R G S L L ACCTGTGGCTCCAGCGATCTGTTATCTGGTCACCAGACACGCTGACGTCATCCCTGTGAGAAGGAGGGGGGATAGCAGAGGCTCCCTGCTC

Gene : HepCla Segment# : 77 Offset : 1141 1st Codon : 1

1st Codon: 1

V I P V R R R G D S R G S L L S P R P I S Y L K G S S G C P
GTGATTCCCGTCAGGAGAAGGGGAGACTCCAGGGGAAGCCTCTTTCCCCCAGACCCATTAGCTATCTGAAAGGCTCCAGGGGAGGCCCT

Gene : HepCla Segment# : 78 Offset : 1156 1st Codon : 1

1st Codon: 1
S P R P I S Y L K G S S G G P L L C P A G H A V G I F R A A
AGCCCTAGGCCTATCTCCTACCTCAAGGGAAGCTCCGGCGGACCCCTCCTGTGTCCCGCCATGCCGTCGGCATTTTCAGAGCCGCT

Gene : HepCla Segment# : 79 Offset : 1171 1st Codon : 1

L L C P A G H A V G I P R A A V C T R G V A K A V D P I P V CTGCTCTGCCGGACACGCTGTGGGAATCTTTAGGGCTGCCGTCTGCACAAGGGGAGTGGCTAAGGCTGTGGATTTCATTCCCGTC

Gene : HepCla Segment# : 80 Offset : 1186 1st Codon : 1

V C T R G V A K A V D P I P V B N L B T T M R S P V P T D N GTGTGTACCAGAGGCGTCGCCAAAGCCGTCGACATTATCCCTGTGGAAAACCTCGAGACAACCATGAGGTCCCCCGTCTTCACAGACAAT

Gene : HepCla Segment# : 81 Offset : 1201 1st Codon : 1

ENLETTMRSPVPTDNSSPPAVPQSFQVAHL
GAGAATCTGGAAACCACAATGAGAAGCCCTGTGTTTACCGATAACTCCAGCCCTCCGGTGTGCCTCAGTCCTTCCAAGTGGCTCACCTC

Gene : HepCla Segment# : 82 Offset : 1216 1st Codon : 1

Gene : HepCla Segment# : 83 Offset : 1231 1st Codon : 1

HAPTGSGKSTKVPAAYAAQGYKVLVLNPSVCACGCTCCCACAGGCTCCCACAGGCTCCCGCAAAAGTCCCCACAAGGTCCCCGCTGCCTATGCCGCTCAGGGATACAAAGTGCTCGTGCTCAACCCTAGCGTC

Gene : HepCla Segment# : 84 Offset : 1246 1st Codon : 1

Y A A Q G Y K V L V L N P S V A A T L G F G A Y M S K A H G
TACGCTGCCCAAGGCTATAAGGTCCTGGATCCCTCACGGAGCCTACAGGAGCCTATATGTCCAAGGCTCACGGA

Gene : HepCla Segment# : 85 Offset : 1261

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1st Codon : 1 A A T L G F G A Y M S K A H G I D P N I R T G V R T I T T G GCCGCTACCCTCGGCTTTGGCGCTTACATGAGCAAAGCCCATGGCATTGACCCTAACATTAGGACAGGCGTCAGGACAATCACAACCGGA Gene : HepCla Segment# : 86 Offset : 1276 1st Codon : 1 I D P N I R T G V R T I T T G S P I T Y S T Y G K F L A D G ATCGATCCCAATATCAGAACCGGAGTGAGAACCATTACCACAGGCTCCCCCCATTACCTATAGCACATACGGAAAGTTTCTGGCTGACGGA Gene : HepCla Segment# : 87 : 1291 1st Codon : 1 S P I T Y S T Y G K F L A D G G C S G G A Y D I I I C D E C AGCCCTATCACATACTCCACCTATGGCAAATTCCTCGCCGATGGCGGATGCTCCGGCGGAGCCTATGACATTATCATTTGCGATGAGTGT Gene : HepCla Segment# : 88 Offset : 1306 1st Codon : 1 G C S G G A Y D I I I C D E C H S T D A T S I L G I G T V L GGCTGTAGCGGAGGCGCTTACGATATCATTATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCGGCATTGGCACAGTGCTC : HepCla Segment# : 89 Offset : 1321 1st Codon : 1 H S T D A T S I L G I G T V L D Q A E T A G A R L V V L A T CACTCCACCGATGCCACAAGCATTCTGGGAATCGGAACCGTCCTGGATCAGGCTGAGACAGCCGGAGCCAGACTGGTCGTCGCCACA Gene : HepCla Segment# : 90 Offset : 1336 1st Codon : 1 D Q A E T A G A R L V V L A T A T P P G S V T V P H P N I E GACCAAGCCGAAACCGCTGGCGCTAGGCTCGTGGTCCTGGCTACCCCTCCCGGAAGCGTCACCGTCCCCCATCCCCAATATCGAA Gene : HepCla Segment# : 91 Offset : 1351 1st Codon : 1 ATPPGSVTVPHPNIEEVALSTTGEIPFYGK GCCACACCCCCTGGCTCCGTGACAGTGCCTCACCCTAACATTGAGGAAGTGGCTCTGTCCACCACAGGCGAAATCCCTTTCTATGGCAAA Gene : HepCla Segment# : 92 Offset : 1366 1st Codon : 1 E V A L S T T G E I P P Y G K A I P L E V I K G G R H L I P GAGGTCGCCCTCAGCACACCGGAGAGATTCCCTTTTACGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGCAGACACCTCATCTTT Gene : HepCla Segment# : 93 Offset : 1381 1st Codon : 1 AIPLEVIKGGRHLIFCHSKKKCDELAAKLV GCCATTCCCCTCGAGGTCATCAAAGGCGGAAGGCATCTGATTTTCTGTCACTCCAAGAAAAGTGTGACGAACTGCCGAAACTGGTC : HepCla Gene Segment# : 94 Offset : 1396 1st Codon : 1 C H S K K C D E L A A K L V A L G I N A V A Y Y R G L D V TGCCATAGCAAAAGAATGCGATGAGCTCGCCGATAGCTCGTGGCTCTGGGAATCAATGCCGTCGCCTATTACAGAGGCCTCGACGTC Gene : HepCla Segment# : 95 Offset : 1411 A L G I N A V A Y Y R G L D V S V I P T S G D V V V A T D 

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Gene : HepCla Segment# : 96 Offset : 1426 lst Codon : 1

S V I P T S G D V V V V A T D A L M T G Y T G D F D S V I D AGGGTCATCCCTACCTCCGGCGATGTCGTCGTCGCCACAGACGCTCTGATGACCGGATACACAGGCGGATTTCGATAGCGTCATCGAT

Gene : HepCla Segment# : 97 Offset : 1441 lst Codon : 1

A L M T G Y T G D F D S V I D C N T C V T Q T V D F S L D P GCCCTCATGACAGGCTATACCGGAGACTTTGACTCGTGATTGACTGTTAACACATGCGTCACCCCAAACCGTCGACTTTAGCCTCGACCCT

Gene : : HepCla Segment# : 98 Offset : 1456 1st Codon : 1

C N T C V T Q T V D F S L D P T F T I E T T T L P Q D A V S
TGCAATACCTGTGTGACACAGACAGCGGTGGATTCTCCCTGGATCCCACATTCACAATCGAAACCACAACCCTCCCCCAAGACGCTGTGTCC

Gene : HepCla Segment# : 99 Offset : 1471 1st Codon : 1

T F T I B T T T L P Q D A V S R T Q R R G R T G R G K P G I ACCITTACCATTGAGACCACACTGCCTCAGGATGCCGTCAGGAGCCCAAAGGAGGCGGAAGCCCGGAAGCCTGGCATT

Gene : HepCla Segment# : 100 Offset : 1486 1st Codon : 1

RTQRRGRTGRGKPGIYRFVAPGERPSGMFD

Gene : HepCla
Segment# : 101
Offset : 1501
1st Codon : 1

Y R F V A P G B R P S G M P D S S V L C B C Y D A G C A W Y TACAGATTCGTCGCCCCCTGGCGAAAGGCCCTAGCGGATGTTTGACTCCAGCGTCCTGTTGAGTGTTACGATGCCGGATGCGCTTGGTAT

Gene : HepCla Segment# : 102 Offset : 1516 1st Codon : 1

S S V L C E C Y D A G C A W Y E L T P A E T T V R L R A Y M AGCTCCGTGCGAATGCTATGACGCTGCTGCGGAACTGACACCCGCTGAGACAACCGTCAGGCTCAGGGCTTACATG

Gene : HepCla Segment# : 103 Offset : 1531 1st Codon : 1

BLTPABTTVRLRAYMNTPGLPVCQDHLBFNGAGCTCACCCTGCCAAGACCACTCGGAATCCTGGAGCCTATATGAATACCCCTGGCCTCCCCGTCTGCCAAGACCACTCTGGAATTCTGG

Gene : HepCla Segment# : 104 Offset : 1546 1st Codon : 1

N T P G L P V C Q D H L B P W B G V P T G L T H I D A H P L AACACCCGGACTGCCCTGTGTGAGGACCCCGAGTTTTGGGAAGGCGTCTTCACAGGCCTCACCCATATCGATGCCCATTTCCTC

Gene : HepCla Segment# : 105 Offset : 1561 lat Codom : 1

BGVFTGLTHIDAHFLSQTKQSGBNFFYLVA

Gene : HepCla Segment# : 106

121/216 Offset : 1576 1st Codon : 1 S Q T K Q S G E N F P Y L V A Y Q A T V C A R A Q A P P P S AGCCAAACCAAACAGTCCGGCGAAAACTTTCCCTATCTGGTCGCCTATCAGGCTACCGTCTGCGCTAGGGCTCAGGCTCCCCCTCCC Gene : HepCla Segment# : 107 Offset : 1591 1st Codon : 1 YQATVCARAQAPPPSWDQMWKCLIRLKPTL TACCAAGCCACAGTGTGTGCCAGAGCCCCAAGCCCTCCCCCTAGCTGGGACCAAATGTGGAAGTGTCTGATTAGGCTCAAGCCTACCCTC : НерС1а Segment# : 108 Offset : 1606 1st Codon : 1 W D Q M W K C L I R L K P T L H G P T P L L Y R L G A V Q N TGGGATCAGAATGCCTCATCAGACTGAAACCCACACTGCATGGCCCCTACCCCTCTGCTCTACAGACTGGGAGCCGTCCAGAAT Gene : HepCla Segment# : 109 Offset : 1621 1st Codon: 1
H G P T P L L Y R L G A V Q N E V T L T H P V T K Y I M T C CACGGACCCACACCCCTCCTGTATATGGCTCGGCGCTGTGCAAAACGAAGTGACACTGACACACCCTGTGACAAAGTATATCATGACCTGT : HepCla Segment# : 110 Offset : 1636 1st Codon : 1 B V T L T H P V T K Y I M T C M S A D L E V V T S T W V L V : HepCla Segment# : 111 Offset : 1651 1st Codon : 1 M S A D L E V V T S T W V L V G G V L A A L A A Y C L S T G : HepCla Segment# : 112 Offset : 1666 1st Codon : 1 G G V L A A L A A Y C L S T G C V V I V G R I V L S G K P A GGCGGAGTGCTCGCCGCTCTGGCTGCCTATTGCCTCAGCACAGGCTGTGTGGTCATCGTCGGCAGAATCGTCCTGTCCGGCAAACCCGCT : HepCla Segment# : 113 Offset : 1681 1st Codon : 1 CVVIVGRIVLSGKPAIIPDREVLYREFDEM TGCGTCGTGATTGTGGGAAGGATTGTGCTCAGCGGAAAGCCTGCCATTATCCCTGACAGAGAGGTCCTGTATAGGGAATTCGATGAGATG : HepCla Segment# : 114 Offset : 1696 1st Codon : 1 II P D R B V L Y R B F D B M B B C S Q H L P Y I B Q G M M ATCATTCCCGATAGGGAAGTGCTCTACAGAGAGTTTGACGAAATGGAAGAGTGTAGCCAACACCTCCCCTATATCGAACAGGGAATGATG : HepCla Segment# : 115 Offset : 1711 1st Codon : 1 E B C S Q H L P Y I B Q G M M L A B Q F K Q K A L G L L Q T GAGGAATGCTCCCAGCATCTGCCTTACATTGAGCAAGGCATGATGCTCGCCGAACAGTTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACA Gene : HepCla Segment# : 116 Offset : 1726 1st Codon : 1

Figure 26 (Cont)

LABQPKQKALGLEQTASRQABVIAPAVQTM

# 122/216

Gene : HepCla ·
Segment# : 117
Offset : 1741
1st Codon : 1

A S R Q A B V I A P A V Q T N W Q K L E V F W A K H M W N F GCCTCCAGGCAAGCCGAAGTGATTGCCCCTGCCGTCCAGACAAACTGGCAGAAACTGGCAGAAGTGTTTTGGGCTAAGCATATGTGGAACTTT

Gene : HepCla Segment# : 118 Offset : 1756 1st Codon : 1

W Q K L E V F W A K H M W N F I S G I Q Y L A G L S T L P G TGGCAAAAGCTCGAGGTCTTCTGGGCCAAACACATGTGGAATTCATTAGCGGAATCCAATACCTCGCCGGACTGTCCACCCTCCCCGGA

Gene : HepCla Segment# : 119 Offset : 1771 1st Codon : 1

I S G I Q Y L A G L S T L P G N P A I A S L M A F T A A V T ATCTCCGCCATCAGCATCTCAGCAGCATCCCGCTATCGCTTCACAGCCGCTTGACA

Gene : HepCla Segment# : 120 Offset : 1786 1st Codon : 1

N P A I A S L M A F T A A V T S P L T T S Q T L L F N I L G AACCCTGCCATTGCCTCCTGATGGCCTTTACCGTTTTACCGTCACCTCCCCCTCACCACAACCCTACCTCCTGTTTTAACATTCTGGGA

Gene : HepCla Segment# : 121 Offset : 1801 1st Codon : 1

Gene : HepCla Segment# : 122 Offset : 1816 1st Codon : 1

G W V A A Q L A A P G A A T A F V G A G L A G A A I G S V G GGCTGGGTGGCTGCCCAACTGGCTGCCCTGGCGCTGCCACTGGCACTGGCTGCCGACTGGCTGCCCATTGGCTCCGTGGGA

Gene : HepCla Segment# : 123 Offset : 1831 1st Codon : 1

FVGAGLAGAGCGCTCGCCGGAGCCGCTATCGGAAGCGTCGGCCTCGGCAAAGTGCTCGTGGATATCCTCGCCGGATACGGAGCCCGGA

Gene : HepCla Segment# : 124 Offset : 1846 lst Codon : 1

L G K V L V D I L A G Y G A G V A G A L V A P K I M S G B V CTGGGAAAGGTCCTGGTCGACACTTCTGGCTGGCTTAGGCGGAGGGTCCTGGGCTTTCAAAATCATGAGCGGAGAGGTC

Gene : HepCla Segment# : 125 Offset : 1861 1st Codon : 1

V A G A L V A P K I M S G B V P S T B D L V N L L P A I L S GTGGCTGGCGCTCTGGCCCTTTAAGATTATGTCCGGCGAAGTGCCTAGCACAGAGGATCTGGTCAACCTCCTGCCATTCTGTCC

Gene : HepCla Segment# : 126 Offset : 1876 1st Codon : 1

PSTEDLVNLLPAILSPGALVVGVVCAAILRCCCCCCGAAGACCCCGGAAGACCCCGGAAGACCCCGGAAGACCCCGGAAGACCCCGGCATCCCCCGCTACCCCAGCCCCTGGCGCCCCTGGGGACTGGTCGCGCCCATCCTGAGA

Gene : HepCla

#### 123/216

Segment# : 127 Offset : 1891 1st Codon : 1

Gene : HepCla Segment# : 128 Offset : 1906 1st Codon : 1

R H V G P G B G A V Q W M N R L I A F A S R G N H V S P T H
AGGCATGTGGGACCCGGAGGGGAGCCGTCCAGTGGATGAATAGGCTCATCGCTTTCGCTAGCAGAGGCAATCACGTCAGCCCTACCCAT

Gene : HepCla Segment# : 129 Offset : 1921 1st Codon : 1

L I A P A S R G N H V S P T H Y V P E S D A A A R V T A I L CTGATTGCCTTCGGGGGAAACCATGTGTCCCCCACACACTATGTGCCTGAGTCCGACGCTGCGCTAGGGTCACCGCTATCCTC

Gene : HepCla Segment# : 130 Offset : 1936 1st Codon : 1

Y V P E S D A A A R V T A I L S S L T V T Q L L R R L H Q W TACETCCCCGAAAGCGATGCCGCGGGGGGGGGCATCGGGCATCTGGCGGGGATGCCGACCGCGACTGCCTCACCGACTGCCTCACCGAGGACTGCATCAGTGG

Gene : HepCla Segment# : 131 Offset : 1951 1st Codon : 1

Gene : HepCla Segment# : 132 Offset : 1966 1st Codon : 1

I S S B C T T P C S G S W L R D I W D W I C B V L S D F K T ATCTCCAGCGAATGCACACCCCTTGCTCCGGCTCCTGGCTCAGGGATATCTGGGACTGGACTTGTGAGGTCCTGTCCGACTTTAAGACA

Gene : HepCla Segment# : 133 Offset : 1981 1st Codon : 1

D I W D W I C B V L S D F K T W L K A K L M P Q L P G I P F GACATTTGGGATTGCGAAGTGCTCAGCGATTCCCTTT

Gene : HepCla Segment# : 134 Offset : 1996 1st Codon : 1

W L K A K L M P Q L P G I P F V S C Q R G Y K G V W R G D G TGGCTCAAGGCTAAGGCTAAGGCTCAGCCTCCAGGCGAATCCCTTTCGTCAGCTGTCAGAGGGCTATAAGGGAGTGTGGAGGGGAGACGGA

Gene : HepCla Segment# : 135 Offset : 2011 1st Codon : 1

Gene : HepCla Segment# : 136 Offset : 2026 1st Codon : 1

I M H T R C H C G A B I T G H V K N G T M R I V G P R T C R ATCATGCACACAGGGTGTCACTGTGGCGCTGAGACTTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGAGAA

Gene : HepCla Segment# : 137 Offset : 2041 1st Codon : 1

## 124/216

V K N G T M R I V G P R T C R N M W S G T P P I N A Y T T G GTGAAAAACGGAACCATGAGGATTGTGGGACCCAGAACCTGTAGGAATATGTGGAGCGGAACCTTTCCCATTAACGCTTACACAACCGGA Gene : HepCla Segment# : 138 Offset : 2056 1st Codon : 1 N M W S G T P P I N A Y T T G P C T P L P A P N Y T P A L W AACATGTGGTCCGGCACATTCCCTATCAATGCCTATACCACAGGCCCTTGCACACCCCTCCCCGCTCCCAATTACACATTCGCTCTGTGG Gene : HepCla Segment# : 139 : 2071 1st Codon : 1 PCTPLPAPNYTPALWRVSAEEYVEIRRVGD CCCTGTACCCCTCTGCCCCTAACTATACCTTTGCCCTCTGGAGAGTGTCCGCCGAAGAGTATGTGGAAATCAGAAGGGTCGGCGAT : HepCla Gene Segment# : 140 Offset : 2086 1st Codon : 1 RVSABBYVEIRRVGDFHYVTGMTTDNLKCP AGGGTCAGCGCTGAGGAATACGTCGAGATTAGGAGAGTGGGAGACTTTCACTATGTGACAGGCCATGACCACAGACAATCTGAAATGCCCT : HepCla Segment# : 141 Offset : 2101 1st Codon : 1 PHYVTGMTTDNLKCPCQVPSPBFFTELDGV TTCCATTACGTCACCGGAATGACAACCGATAACCTCAAGTGTCCCTGTCAGGTCCCCTCCCCCGAATTCTTTACCGAACTGGATGGCGTC Gene : HepCla Segment# : 142 : 2116 1st Codon : 1 CQVPSPEPPTELDGVRLHRFAPPCKPLLRE Gene : HepCla Segment# : 143 Offset : 2131 1st Codon : 1 R L H R F A P P C K P L L R E B V S F R V G L H E Y P V G S AGGCTCCACAGATTCGCTCCCCTTGCAAAACCCCTCCTGAGAGAGGAAGTGTCCTTCAGAGTGGGACTGCATGAGTATCCCGTCCGCCTCC Gene : HepCla Segment# : 144 Offset : 2146 1st Codon : 1 EVSPRVGLHBYPVGSQLPCEPBPDVAVLTS GAGGTCAGCTTTAGGGTCGGCCTCCACGAATACCCTGTGGGAAGCCCAACTGCCTTGCGAACCCGAACCCGATGTGGCTGTGCTCACCTCC : HepCla Gene Segment# : 145 : 2161 Offset 1st Codon : 1 Q L P C E P E P D V A V L T S M L T D P S H I T A E A A G R CAGCTCCCCTGTGAGCCTGACGTCGCCGTCCTGACAAGCATGCTGACAAGCCCTAGCCATATCACAGCCGAAGCCGCTGGCAGA Gene : HepCla Segment# : 146 : 2176 1st Codon : 1 M L T D P S H I T A E A A G R R L A R G S P P S M A S S S A ATGCTCACCGATCCCTCCCACATTACCGCTGAGGCTGCCGGAAGGAGACTGGCTAGGGGAAGCCCTCCCACGCTAGCTCCAGGGCT Gene : HepCla Segment# : 147 Offset : 2191 1st Codon : 1 R L A R G S P P S M A S S S A S Q L S A P S L K A T C T A N 

# 125/216

Gene : HepCla Segment# : 148 Offset : 2206 lst Codon : 1

S Q L S A P S L K A T C T A N H D S P D A E L I E A N L L W AGCCAACTGTCCGCCCCTAGCCTCAGGCTACCCTCTTGCGCTAACCATGACTCCCCCGATGCCGAACTGATTGAGGCTAACCTCCTGTGG

Gene : HepCla Segment# : 149 Offset : 2221 1st Codon : 1

H D S P D A E L I B A N L L W R Q E M G G N I T R V E S E N CACGATAGCCCTGAGCTCGAGGCCAATCTGCTCTGGAGACAGGGAAATGGGAGCCAATATCACAAGGGTCGAGTCCGAGAAT

Gene : HepCla Segment# : 150 Offset : 2236 1st Codon : 1

R Q E M G G N I T R V E S E N K V V I L D S F D P L V A E E AGGCAAGAGATGGGCGGAAACAATTACCAGAGTGGAAAGCGAAACAAGTGGTCATCCTCGACTCCTTCGATCCCTCGTGGCTGAGGAA

Gene : HepCla Segment# : 151 Offset : 2251 1st Codon : 1

K V V I L D S F D P L V A E B D B R E I S V P A E I L R K S AAGGTCGTGATTCTGGATAGCTCTCGGAAAGTCC

Gene : HepCla Segment# : 152 Offset : 2266 lst Codon : 1

Gene : HepCla Segment# : 153 Offset : 2281 1st Codon : 1

R R P A Q A L P V W A R P D Y N P P L V E T W K K P D Y E P AGGAGATTCGCTCAGGCTCTGCCTGTGGGGCCAGACCCGATTACAATCCCCCTCTGGTCGACAAAAAGCCTGACTATGAGCCT

Gene : HepCla Segment# : 154 Offset : 2296 1st Codon : 1

N P P L V B T W K K P D Y B P P V V H G C P L P P P R S P P AACCCTCCCCTCGGAAACCCCGATTACGAACCCCCTGTGGTCCACGGATGCCCTCTGCCTCCCCCTAGGTCCCCCCCT

Gene : HepCla Segment# : 155 Offset : 2311 1st Codon : 1

Gene : HepCla Segment# : 156 Offset : 2326 1st Codon : 1

V P P P R K K R T V V L T B S T L S T A L A B L A T K S P G GTGCCTCCCCTAGGAAAAAGGGAACCGTCGTCCACCGAAAGCACCTCTCCGCA

Gene : HepCla Segment# : 157 Offset : 2341 1st Codon : 1

T L S T A L A E L A T K S P G S S S T S G I T G D N T T T S ACCUTCAGCACAGCCCTCGGCACACATGCCTACCACAAAGCTTTGGCTCCAGCTCCACCTCCGGCACTTACCGGAGACAATACCACAAACCTCC

Gene : HepCla Segment# : 158 Offset : 2356

126/216 1st Codon : 1 S S S T S G I T G D N T T T S S B P A P S G C P P D S D A E AGCTCCAGCACAAGCGGAATCACAGGCGATAACACAACCACCAGGCTCCGAGCCTGCCCCTAGCGGATGCCCTCCCGATAGCGATGCCGATA : HepCla Segment# : 159 Offset : 2371 1st Codon : 1 SEPAPS GCPPD SDAESYSSMPPLEGEPGD P AGCGAACCCGCTCCCTCCGGCTGTCCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCCTCTGGAAGGCGAACCCCGAGGACCCT : HepCla Gene Segment# : 160 Offset : 2386 1st Codon : 1 S Y S S M P P L E G E P G D P D L S D G S W S T V S S E A G AGCTATAGCTCCATGCCTCCCTCGAGGGAGAGCCTGGCGATCCCGATCTCTCCGACGGAAGCTGGAGGAAGCTGTCCAGCGAAGCCGGA : HepCla Gene Segment# : 161 Offset : 2401 1st Codon : 1 D L S D G S W S T V S S E A G T E D V V C C S M S Y S W T G GACCTCAGCGATGGCTCCTGGTCCACCTCAGCTCCGAGGCTGGCACAGAGGATGTGGTCTGCTGTAGCATGAGCTATAGCTGGACCGGA Gene : HepCla Segment# : 162 Offset : 2416 1st Codon : 1 T E D V V C C S M S Y S W T G A L V T P C A A E E Q K L P I ACCGAAGACGTCGTGTGTTGCTCCATGTCCTACTCCTGGACAGGCGCTCTGGTCACCCCTTGCGCTGCCGAAGAGCCAAAAGCTCCCCATT Gene : HepCla Segment# : 163 Offset : 2431 1st Codon : 1 A L V T P C A A E E Q K L P I N A L S N S L L R H H N L V Y GCCCTCGTGACACCCTGTGCCGCTGAGGAACAGAAACTGCCTATCAATGCCCTCAGCAATAGCCTCCTGAGACACCATAACCTCGTGTAT Gene : HepCla Segment# : 164 Offset : 2446 1st Codon : 1 N A L S N S L L R H H N L V Y S T T S R S A C Q R Q K K V T : HepCla Gene Segment# : 165 Offset : 2461 1st Codon : 1 S T T S R S A C Q R Q K K V T F D R L Q V L D S H Y Q D V L AGCACAACCTCCAGGTCCGCCTGTCAGAGACAGAAAAAGGTCACCTTTGACAGACTGCAAGTGCTCGACTCCCACTATCAGGATGTGCTC Gene : HepCla Segment# : 166 Offset : 2476 1st Codon : 1 FDRLQVLDSHYQDVLKBVKAAASKVKANLL TTCGATAGGCTCCAGGTCCTGGATAGCCATTACCAAGACGTCCTGAAAGAGGTCAAGGCTGCCGCTAGCAAAGTGAAAGCCAATCTGCTC : HepCla Gene Segment# : 167 Offset : 2491 1st Codon : 1 K E V K A A A S K V K A N L L S V E E A C S L T P P H S A K AAGGAAGTGAAAGCCGCTGCCTCCAAGGTCAAGGCTAACCTCCTGTCCGTGGAAGAGGGCTTGCTCCCTGACACCCCCTCACTCCGCCAAA Gene : HepCla Segment# : 168 Offset : 2506 1st Codon : 1

Figure 26 (Cont)

S V B B A C S L T P P H S A K S K P G Y G A K D V R C H A R AGCGTCGAGGAGCCTGTAGCCTCACCCCCCCCCATAGCGCTAAGTTTTGGCTATGCCGCTAAGGATGTAGATCCCATGCCAGA

## 127/216

Gene : HepCla Segment# : 169 Offset : 2521 1st Codon : 1

S K F G Y G A K D V R C H A R K A V A H I N S V W K D L L E AGCAAATTCGGATACGGAGCCAAAGACGTCAGGTGTCACGCTAGGAAAGACCTCCTGGAA

Gene : HepCla Segment# : 170 Offset : 2536 lst Codon : 1

KAVAHINSVWKDLLEDSVTPIDTTIMAKNE AAGGCTGTGGCTCACCCCTATCGATACCACAATCATGGCCAAAAACGAA

Gene : HepCla Segment# : 171 Offset : 2551 1st Codon : 1

D S V T P I D T T I M A K N B V P C V Q P B K G G R K P A R GACTCCGTGACACCCATTGACACCACTTATGGCTAAGAATGAGTCTTCTGTGTGCAACCCGAAAAGGGAGGCAGAAAGCCTGCCAGA

Gene : HepCla Segment# : 172 Offset : 2566 1st Codon : 1

Gene : HepCla Segment# : 173 Offset : 2581 1st Codon : 1

LIVFPDLGVRVCEKMALYDVVSKLPLAVMGCTGATTGTGTTTCCCGATCTCGGAGTGTGTGAGAAATGGCTCTGTATGACGTCCTGTCCCAGCTCCCCCTCGCCGTCATGGGA

Gene : HepCla Segment# : 174 Offset : 2596 1st Codon : 1

A L Y D V V S K L P L A V M G S S Y G F Q Y S P G Q R V B F GCCCTCTACGATGTGGTCAGCAAACTGCCTCTGGCTGATGGGCTCCAGCTATGGCTTTCAGTATAGCCCTGGCCAAAGGGTCGAGTTT

Gene : HepCla Segment# : 175 Offset : 2611 1st Codon : 1

S S Y G F Q Y S P G Q R V B F L V Q A W K S K K T P M G F S AGCTCCTACGGATTCCCAGGAGACCCCTATGGGATTCTCC

Gene : HepCla Segment# : 176 Offset : 2626 1st Codon : 1

L V Q A W K S K K T P M G F S Y D T R C P D S T V T E S D I CTGGTCCAGGCTTGGAAAAGCAAAAAGACCCCATGGCTTTAGCTATGACACAAGGTGTTTCGATAGCACAGTGACACAGT

Gene : HepCla Segment# : 177 Offset : 2641 1st Codon : 1

Y D T R C F D S T V T B S D I R T B B A I Y Q C C D L D P Q TACGATACCAGATGCTTTGACTCCCACGTCACCGAAAGCGATATCAGAACCGAAGAGGCTATCTTATCAGTGTTGCGATCTCGATCCCCAA

Gene : HepCla Segment# : 178 Offset : 2656 1st Codon : 1

Gene : HepCla Segment# : 179

#### 128/216

Offset : 2671 1st Codon : 1 A R V A I K S L T E R L Y V G G P L T N S R G E N C G Y R R GCCAGAGTGGCTATCAAAAGCCTCACCGAAAGGCTCTACGTCGGCGGACCCCTCACCAATAGCAGAGGCGAAAACTGTGGCTATAGGAGA Gene : HepCla Segment# : 180 Offset : 2686 1st Codon : 1 G P L T N S R G B N C G Y R R C R A S G V L T T S C G N T L GGCCCTCTGACAAACTCCAGGGGAGAGAATTGCGGATACAGAAGGTGTAGGGCTAGCGGAGTGCTCACCACAAGCTGTGGCAATACCCTC Gene : HepCla Segment# : 181 Offset : 2701 1st Codon : 1 C R A S G V L T T S C G N T L T C Y I K A R A A C R A A G L TGCAGAGCCTCCGGCGTCCTGACAACCTCCTGCGGAAACACACTGACATGCTATATCAAAGCCAGAGCCGCTTGCAGAGCCGCTGGCCTC : HepCla Segment# : 182 Offset : 2716 1st Codon : 1 T C Y I K A R A A C R A A G L Q D C T M L V C G D D L V V I ACCTGTTACATTAAGGCTAGGGCTGCCTGTAGGGCTGCCGGACTGCAAGACTGTACCATGCTGGTCGCGGAGACGATCTGGTCGTGATT : HepCla Segment# : 183 Offset : 2731 1st Codon: 1 Q D C T M L V C G D D L V V I C E S A G V Q E D A A S L R A CAGGATTGCACAATGCTCGTGTGTGGCGATGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGCCCCTAGCCTCAGGGCT Gene : HepCla Segment# : 184 : 2746 Offset 1st Codon : 1 C E S A G V Q E D A A S L R A F T E A M T R Y S A P P G D P TGCGAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCCTGAGAGCCTTTACCGAAGCCATGACCAGATACTCCGGCCCTCCCGGAGACCCT Gene : HepCla Segment# : 185 Offset : 2761 1st Codon : 1 F T E A M T R Y S A P P G D P P Q P E Y D L E L I T S C S S TTCACAGAGGCTATGACAAGGTATAGCGCTCCCCCTGGCGATCCCCCTCAGCCTGAGTATGACCTCGAGCTCATCACAAGCTGTAGCTCC Gene : HepCla Segment# : 186 Offset : 2776 1st Codon : 1 PQPBYDLELITSCSSNVSVAHDGAGKRVYY CCCCAACCCGAATACGATCTGGAACTGATTACCTCCTGCTCCAGCAATGTGTCCGTGGCTCACGATGGCGCTGGCAAAAGGGTCTACTAT Gene : HepCla Segment# : 187 : 2791 1st Codon: 1 N V S V A H D G A G K R V Y Y L T R D P T T P L A R A A W E : HepCla Gene Segment# : 188 : 2806 Offset 1st Codon: 1 LTRDPTTPLARAAWETARHTPVNSWLGNII  $\tt CTGACAAGGGATCCCACAACCCCTCTGGCTAGGGCTGCCTGGGAGACAGCCAGACACCCCGTCAACTCCTGGCTCGGCAATATCATT$ : HepCla Segment# : 189 Offset : 2821 1st Codon : 1 TARHTP V N S N L G N I I M P A P T L W A R M I L M T H

## 129/216

ACCGCTAGGCATACCCCTGTGAATAGCTGGCTGGGAAACATTATCATGTTCGCTCCCACACTGTGGGCCAGAATGATTCTGATGACCCAT

Gene : HepCla Segment# : 190 Offset : 2836 1st Codon : 1

M F A P T L W A R M I L M T H F F S V L I A R D Q L E Q A L ATGITTGCCCCTACCCTCTGGGCTGGGCTGACGCTCGACGACCCCTC

Gene : HepCla Segment# : 191 Offset : 2851 1st Codon : 1

PPSVLIARDQLEQALDCBIYGACYSIEPLD

Gene : HepCla Segment# : 192 Offset : 2866 lst Codon : 1

D C E I Y G A C Y S I E P L D L P P I I Q R L H G L S A P S GACTGTGAGATTTACGGAGCCTGTTACTCCATCGAACCCCTCGACCTCCCCCCTATCATTCAGAGACTGCATGGCCTCAGCGCTTTCTCCC

Gene : HepCla Segment# : 193 Offset : 2081 1st Codon : 1

LPPIIQRLHGLSAPSLHSYSPGBINRVAACCTGCCTCCCATTATCCAAAGGCTCCACGGACGATTAACAGAGTGGCTGCCTGT

Gene : HepCla Segment# : 194 Offset : 2896 1st Codon : 1

L H S Y S P G E I N R V A A C L R K L G V P P L R A W R H R CTGCATAGCTATAGCCCTGGCGAAATCAATAGGGTCGCCGCTTGCCTCAGGAAACTGGGAGACTGCGCTCCCCTCAGGACACAGA

Gene : HepCla Segment# : 195 Offset : 2911 1st Codon : 1

LRKLGVPPLRAWRHRARSVRARLLARGGRAACTGGGGGAGGGGGAGGGCTAGGGCTAGGCCTGGAGAGCCAGACTGCTCGCCAGAGGCGGAAGGGCT

Gene : HepCla Segment# : 196 Offset : 2926 1st Codon : 1

A R S V R A R L L A R G G R A A I C G K Y L F N W A V R T K GCCAGAAGCGTCAGGGCTCAGGGCTCAGGGGGGGGGGGCAGAGCCGCTATCTGGGCAAATACCTCTTCAATTGGGCTGTGAGAACCAAA

Gene : HepCla Segment# : 197 Offset : 2941 1st Codon : 1

A I C G K Y L P N W A V R T K L K L T P I A A A G R L D L S GCCATTTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAGCTCAAGCTCACCCCTATCGCTGCCGCTGGCAGACTGGATCTGTCC

Gene : HepCla Segment# : 198 Offset : 2956 1st Codon : 1

Gene : HepCla Segment# : 199 Offset : 2971 1st Codon : 1

G W F T A G Y S G G D I Y H S V S H A R P R W F W F C L L L GGCTGGTTCACAGCCGGATACTCCGGCGGGACACTTTACCATAGCGTCAGCCATGCCAGACCCAGATGGTTTTGGTTTTGCCTCCTGCTC

Gene : HepCla

#### 130/216

Segment# : 200 Offset : 2986 1st Codon : 1

V S H A R P R W F W F C L L L A A G V G I Y L L P N R A A GTGTCCCACGCTAGGCGTAGGTGGTTCTGGTTCTGCTCCTGCTCGCCGCTGGCGTCGCCATTTACCTCCTGCCTAACAGAGCCGCT

Gene : HepCla Segment# : 201 Offset : 3001 1st Codon : 1

L A A G V G I Y L L P N R A A CTGGCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCC

Segments in scrambled order:

\_\_\_\_\_

HepCla #77

V I P V R R R G D S R G S L L S P R P I S Y L K G S S G G P GTGATTCCCGTCAGGGAGAGGCTCCAGGGGAGGCCCCTTTCCCCCAGACCCATTAGCTATCTGAAAGGCTCCAGCGGAGGCCCCT

HepCla #68

A R R G R E I L L G P A D G M V S K G W R L L A P I T A Y A GCCAGAAGGGGAAGGGAAATCCTCCTGGGACCCCCTGACGGATGGTCAGCAAAGGCTGGAGGCTCCTGCCTCCCATTACCGCTTACGCT

HepCla #143

R L H R F A P P C K P L L R B B V S F R V G L H B Y P V G S AGGCTCCACAGATTCGCTCCCCTTGCAAACCCCTCCTGAGAGAGGAAGTGTCCTTCAGAGTGGGACTGCATGAGTATCCCGTCGGCTCC

HepCla #66

V V F S Q M E T K L I T W G A D T A A C G D I I N G L P V S GTGGTCTTCTCCCAGATGGAGACAAAGCTCATCACTAGGGAGCCGATACCGCTGCCTGTGGCGATACATTAACGGACTGCCTGTGTCC

HepCla #79

L L C P A G H A V G I F R A A V C T R G V A K A V D P I P V CTGCTCTGCCCTGCCGGACACGCTGTGGGATTTCATTCCCGTC

HepCla #113

C V V I V G R I V L S G K P A I I P D R E V L Y R E P D E M
TGCGTCGTGATTGTGGGAAGGATTGTGCTCAGCGGAAAGCCTGCCATTATCCCTGACAGAGAGGTCCTGTATAGGGAATTCGATGAGATG

HenCla #139

PCTPLPAPNYTPALNRVSAEEYVEIRRVGD

HepCla #174

A L Y D V V S K L P L A V M G S S Y G F Q Y S P G Q R V B P GCCCTCTACGATGTGGTCAGCAAACTGCCTCTGGCTGTGATGGGCTCCAGCTATGGCTTTCAGTATAGCCCTGGCCAAAGGGTCGAGTTT

HepCla #57

I S W C L W W L Q Y F L T R V B A Q L H V W V P P L N V R G ATCTCCTGGTGTCTGGGTGCTCCAGTATTTCCTCACCAGAGTGGAAGCCCAACTGCATGTGTGGGTGCCTCCCCTCAACGTCAGGGGA

HepCla #51

BNLVILNAASLAGTHGLVSFLVFFCFAWYL

HepCla #193

L P P I I Q R L H G L S A F S L H S Y S P G E I N R V A A C CTGCCTCCCATTATCCCAAGGGTCCACGGGACTGTCCGCCTTTAGCCTCCCCCCGGAGAGTTAACAGAGTGGCTGCTGT

HepCla #154

N P P L V E T W K K P D Y E P P V V H G C P L P P P R S P P AACCCTCCCCTGGGAAACCTGGAAACCCCGATTACGAACCCCCTTGGGTCCACGGATGCCCTCTGCCTCCCCCTAGGTCCCCCCCT

HepCla #48

HepCla #37

HepCla #185

F T E A M T R Y S A P P G D P P Q P E Y D L E L I T S C S S

# 131/216

TICACAGAGGCTATGACAAGGTATAGCGCTCCCCTGGCGATCCCCCTCAGCCTGAGTATGACCTCGAGCTCATCACAAGCTGTAGCTCC

HepCla #54

W P L L L L L A L P Q R A Y A L D T E V A A S C G G V V L TGGCCTCTGCTCCTGCTCCTCCCCCCAAAGGGCTTACGCTCTGGATACCGAAGTGGCTGCTCCTCCTGCTGCTGCTCCTC

HepCla #70

QQTRGLLGCIITSLTGRDKNQVEGEVQIVS CAGCAAACCAGAGGCCTCCTGGGATGCATTATCACAAGCCTCACGGAAGGGATAAGAATCAGGTCGAGGGAGAGGTCCAGATTGTGTCC

HepCla #82

HepCla #104

NTPGLPVCQDHLBFWEGVFTGLTHIDAHFL AACACACCCGGACTGCCTGTGTGAGGATCACCTCGAGTTTTGGGAAGGCGTCTTCACAGGCCTCACCCATATCGATGCCCATTTCCTC

HepCla #26

HepCla #110

HepCla #56

V G L M A L T L S P Y Y K R Y I S W C L W W L Q Y F L T R V GTGGGACTGATGGCCCTCAGCCCTTACTATAAGAGATACATTAGCTGGTGCCTCTGGTGGCTGCAATACTTTCTGACAAGGGTC

HepCla #197

A I C G K Y L P N W A V R T K L K L T P I A A A G R L D L S GCCATTTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAAGCTCAAGCTCACCCCTATCGCTGCCGCTGGCAGACTGGATCTGTCC

HepCla #25

I A Y P S M V G N W A K V L V V L L P A G V D A B T H V T ATCECTTACTITECCEGATGCCGAAACTGCCCAAACTGCTCCTGCTCCTGCTCTGTTTGCCGGAGTGCAGACCCATGTGACA

HepCla #147

R L A R G S P P S M A S S S A S Q L S A P S L K A T C T A N
AGGCTCGCCAGGGCTCCCGCCTCCAGCTCCAGCTCCAGCTCCCTGAAAGCCACATGCACAGCCAAT

HepCla #52

G L V S P L V P P C P A W Y L K G R W V P G A V Y A L Y G M GGCCTCGTGTCCTCCTGTTTTCGCTTGGTATCGCATGGGTCCCCGGGGCCCGTCTACGCTCTGTATGGCATG

HepCla #145

Q L P C B P B P D V A V L T S M L T D P S H I T A B A A G R CAGCTCCCCTGTGAGCCTGACGAGCCTGCCTGACAAGCATGCCTGACAAGCCTTAGCATATCACAGCCGAAGCCGCTGCCAGA

HepCla #171

D S V T P I D T T I M A K N E V P C V Q P B K G G R K P A R GACTCCGTGACACCCATTGACACCATTATGGCTAAGAATGAGGTCTTCTGTGTGCAACCCGAAAAGGGAGGCAGAAAGCCTGCCAGA

HepCla #84

Y A A Q G Y K V L V L N P S V A A T L G P G A Y M S K A H G TACGCTGCCCAAGGCTATAAGGTCCTGGATCCCTGGATCCCTGCGGAGCCTATATGTCCAAGGCTCACGGA

HepCla #14

HepCla #175

S S Y G P Q Y S P G Q R V B F L V Q A N K S K K T P M G P S AGCTCCTACGGATTCCAAGAAAACCCCTATGGGATTCTCC

HepCla #67

HepCla #148

S Q L S A P S L K A T C T A N H D S P D A E L I E A N L L W AGCCAACTGTCCCCCCTAGCCTCAGGCTACCTGTACCGCTAACCATGACTCCCCCGATGCCGAACTGATTGAGGCTAACCTCCTGTGG

#### 132/216

HepCla #120

HepCla #176

L V Q A W K S K K T P M G P S Y D T R C P D S T V T E S D I CTGGTCCAGGCTTGGAAAAGCAAAAAGCCCATGGGCTTTAGCTATGACACAAGGTGTTTCGATAGCACAGTGACAGAGTCCGACATT

HepCla #152

DEREISVPAEILRKSRRFAQALPVWARPDY
GACGAAAGGGAAATCTCCGTGCCTGCCCGAATCCTCAGGAAAGGAAAGGTTTGCCCAAGCCCTCCCGGTCTGGGCTAGGCCTGACTAT

HepCla #190

M P A P T L W A R M I L M T H P P S V L I A R D Q L E Q A L ATGTTTGCCCCTACCCTCTGGGCTAGGCTCATGACACCCTCTCTTTTCTCCGTGCTCATCGCTAGGGATCAGCTCGAGCAGCCCTC

HepCla #96

S V I P T S G D V V V V A T D A L M T G Y T G D P D S V I D AGCGTCATCCCTACCTCCGCCGATGTCGTCGTCGCCACAGACGCTCTGATGACCGGATACACAGGCGGATTTCGATAGCGTCATCGAT

HepCla #94

HepCla #46

HepCla #53

HepCla #87

S P I T Y S T Y G K P L A D G G C S G G A Y D I I I C D E C
AGCCCTATCACATACTCCACCTATGGCAAATTCCTCGCCGATGGCGGATGCTCCGGCGGAGCCTATGACATTATCATTTGCGATGAGTGT

HepCla #196

A R S V R A R L L A R G G R A A I C G K Y L F N W A V R T K
GCCAGAAGCGTCAGGGCTAGGCTAGGGCAGAGCCAGAGCCGCTATCTGTGGCAAATACCTCTTCAATTGGGCTGTGAGAACCAAA

HepCla #170

KAVAHINSVWKDLLEDSVTPIDTTIMAKNB AAGGCTGTGGCTCACATTAACTCCGTGGGAGGATCTGCTCGAGGATGCGTCACCCCCTATCGATACCACAATCATGGCCAAAAACGAA

HepCla #35

PTPSPVVVGTTDRSGAPTYSWGANDTDVPVTTCACACCCTCCCCGTCGTCGGCACACCGATAGGTCCGGCGCTCCCACATACTCCTGGGGAGCCAATGACACAGACGTCTTCGTC

HepCla #16

PGCVPCVREGNASRCWVAMTPTVATRDGKLCCCGGATGCGTCCCCTCTGTGAGAGGGAAACGCTAGCAGATGCTGGGTGGCTATGACACCCACAGTGGCTACCAGAGAGCTCCCCGATGCTGCTGCTGCTTGAGAGAGGGAAACGCTACCAGAGAGGAGAGCTC

HepCla #183

Q D C T M L V C G D D L V V I C E S A G V Q E D A A S L R A CAGGATTGCACAATGCTCGTGGGGATGACCTCGTGGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGCCGCTAGCCTCAGGGCT

HepCla #125

HepCla #177

HepCla #103

BLTPABTTVRLRAYMNTPGLPVCQDHLBPWGAGCTCACCCCTGCCGAAACCACAGGAGCCTATATGAATACCCCTGGCCTCCCCGTCTGCCAAGACCACTCTGGAATTCTGG

HepCla #186

PQPBYDLBLITSCSSHVSVAHDGAGKRVYYCCCCAACCCGAATCGGTCTCGGAATCGGTCTCCTGCTCCAGCAATGTGTCCGTGGCTCACGATGGCGCTGGCAAAAGGGTCTACTAT

#### 133/216

HepCla #9

LGKVIDTLTCGFADLMGYIPLVGAPLGGAA  $\tt CTGGGAAAGGTCATCGATACCCTCACCTGTGGCTTTGCCGATCTGATGGGCTATATCCCTCTGGTCGGCGCTCCCCTCGGCGGAGCCGCT$ 

A I P L E V I K G G R H L I P C H S K K K C D B L A A K L V  ${\tt GCCATTCCCCTCGAGGTCATCAAAGGCCGAAGGCATCTGATTTTCTGTCACTCCAAGAAAAGTGTGACGGACTGGCTGAACTGGTC}$ 

G G V L A A L A A Y C L S T G C V V I V G R I V L S G K P A GGCGGAGTGCTCGCCGCTCTGGCTATTGCCTCAGCACAGGCTGTGTGGTCATCGTCGGCAGAATCGTCCTGTCCGGCAAACCCGCT

HepCla #184

C B S A G V Q B D A A S L R A F T B A M T R Y S A P P G D P TGCGAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCCTGAGAGGCCTTTACCGAAGCCATGACCAGATACTCCGCCCCTCCCGGAGACCCT

G W P T A G Y S G G D I Y H S V S H A R P R W P W P C L L L GGCTGGTTCACAGCCGGATACTCCGGCGGAGACATTTACCATAGCGTCAGCCATGCCAGACCCAGATGGTTTTGGTTTTGCCTCCTGCTC

S S S T S G I T G D N T T T S S E P A P S G C P P D S D A R AGCTCCAGCACAAGCGGAATCACAGCGGATAACACAACCACAAGCTCCGAGCCTGCCCCTAGCGGATGCCCTCCCGATAGCGATGCCGAA

HepCla #100

RTQRRGRTGRGKPGIYRPVAPGERPSGMPD AGGACACAGAGAAGGGGAAGGACAGGCAAACCCGGAATCTATAGGTTTGTGGCTCCCGGAGAGACCCCTCCGGCATGTTCGAT

V R M Y V G G V E H R L E A A C N W T R G E R C D L E D R D GTGAGAATGTATGTGGGAGGCGTCGAGCATAGGCTCGAGGCTGCCTGTAACTGGACCAGAGGCGAAAGGTGTGACCTCGAGGATAGGGAT

EAQLHVWVPPLNVRGGRDAVILLMCVVHPT GAGGCTCACGTCTGGGTCCCCCCTCTGAATGTGAGAGGCGGAAGGGATGCCGTCATCCTCCTGATGTGCGTCGTCCATCCCACA

L G V R A T R K T S B R S Q P R G R R Q P I P K A R R P B G CTGGGAGTGAGAGCCACAAGGAAAACCTCCGAGAGAAGCCAACCCAGAGGCAGAAGGCAACCCATTCCCAAAGCCAGAAGGCTGAGGGA

HepCla #187

N V S V A H D G A G K R V Y Y L T R D P T T P L A R A A W R AACGTCAGCGTCGCCCATGACGGAGCCGGAAAGAGAGTGTATTACCTCACCAGAGACCCTACCACACCCCTCGCCAGAGCCGCTTGGGAA

S E P A P S G C P P D S D A E S Y S S M P P L E G E P G D P AGCGAACCCGCTCCCGCCTGTCCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCCTCTGGAAGGCGAACCCGAGAGACCCT

HepCla #63

IGGHYVQMAIIKLGALTGTYVYNHLTPLRD ATCGGAGGCCATTACGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACCGGAACCTATGTGTATAACCATCTGACACCCCTCAGGGAT

HepCla #126

PST B D L V N L L P A I L S P G A L V V G V V C A A I L R CCCTCCACCGAAGACCTCGTGAATCTGCCCCGCTATCCTCAGCCCTGGCGCTCTGGTCGTGGGAGTGGTCTGCGCTGCCATTCTGAGA

I L D M I A G A H W G V L A G I A Y P S M V G N W A K V L V 

HepCla #7

BGCGWAGWLL SPRGSRPSWGPTDPRRRSRN GAGGGATGCGGATGGGCTGGCTGGCTCAGCCCTAGGGGAAGCAGACCCTCCTGGGGGACCCACAGACCCTAGGAGAAGGTCCAGGAAT

HepCla #21
W T T Q G C N C S I Y P G H I T G H R M A W D M M M N N S P TGGACAACCCAAGGCTGTAACTGTAGCATTTACCCTGGCCATATCACAGGCCATAGGATGGCCTGGGACATGATGATGAACTGGAGCCCT

VAMTPTVAT.RDGKLPATQLRRHIDLLVGS TGGGTCGCCATGACCCCTACCGTCGCCACAAGGGATGGCAAACTGCCTACCACAGGCTCAGGAGACACATTGACCTCCTGGTCGGCTCC

HepCla #42

## 134/216

R L W H Y P C T I N Y T I P K V R M Y V G G V E H R L E A A AGGCTCTGGCATTACCCTTGCACAATCAATTACACAATCTTTAAGGTCAGGATGTACGTCGGCGGAGTCGAACACAGACTGGAAGCCGGCT

V F C V Q P E K G G R K P A R L I V F P D L G V R V C E K M CTCTTTTCCCTCCAGCCTCAGAAAGGCCGAAAGGAAACCCCGCTAGGCTCATCCTCTCCCTGACCTCGGCGTCAGGGTCTGCGAAAAGATG

HepCla #10

M G Y I P L V G A P L G G A A R A L A H G V R V L E D G V N ATGGGATACATTCCCCTCGTGGGAGCCCCTCTGGGAGGGCGCTGCCAGAGCCCTCGCCCATGGCGTCAGGGTCCTGGAAGACGGAGTGAAT

G G N A G R T T S G L V S L L T P G A K Q N I Q L I N T N G GGCGGAAACGCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCCGGAGCCAAACAGAATATCCAACTGATTAACACAAACGGA

HepCla #13

LALLSCLTVPASAYQVRNSTGLYHVTNDCP  $\tt CTGGCTCTGCTCTGACAGTGCCTGCCTCCGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAAACGATTGCCCT$ 

G R D K N Q V E G E V Q I V S T A A Q T F L A T C I N G V C GGCAGAGACAAAAACCAAGTGGAAGGCGAAGTGCAAATCGTCAGCACACCCGCTCAGACATTCCTCGCCACATGCATTAACGGAGTGTGT

PATQLRRHIDLLVGSALLVGGLCGS CCCGCTACCCAACTGAGAAGGCATATCGATCTGGTCGGGAAGCGCTACCCTCTGCTCCGCCCTCTACGTCGGCGATCTGTGGGCTCC

H A P T G S G K S T K V P A A Y A A Q G Y K V L V L N P S V CACGCTCCCACAGGCTCCGGCAAAAGCACAAAGGTCCCCGCTGCCTATGCCGCTCAGGGATACAAAGTGCTCGTGCTCAACCCTAGCGTC

HepCla #6

R T W A Q P G Y P W P L Y G N R G C G W A G W L L S P R G S 

T B D V V C C S M S Y S W T G A L V T P C A A E E Q K L P I ACCGAAGACGTCGTGTGTGCTCCATGTCCTACTCCTGGACAGGCGCTCTGGTCACCCCTTGCGCTGCCGAAGAGCAAAAGCTCCCCATT

ALDTEVAASCGGVVLVGLMALTLSPYYKRY GCCCTCGACACAGAGGTCGCCGCTAGCTGGCCGAGTGGTCCTGGTCGGCCTCATGGCTCTGACACTGTCCCCCTATTACAAAAGGTAT

N M N S T G F T K V C G A P P C V I G G A G N N T L H C P T 

HepCla #168

S V E B A C S L T P P H S A K S K F G Y G A K D V R C H A R AGCGTCGAGGAAGCCTGTAGCCCTCACCCCTCCCCATAGCGCTAAGTTCCAAGTTTGGCTATGCCGCTAAGGATGTGAGATGCCATGCCAGA

I S G I Q Y L A G L S T L P G N P A I A S L M A P T A A V T ATCTCCGGCATTCAGTATCTGGCTGGCACACTGCCTGGCAATCCCGCTATCGCTAGCCTCATGGCTTTCACAGCCGCTGTGACA

Q I V G G V Y L L P R R G P R L G V R A T R K T S E R S O P CAGATTGTGGGAGGGTCTACCTCCTGCCTAGGAGAGGCCCTAGGCTCAGGGTACCAGAAAGACAAGCGAAAGGTCCCAGCCT

HepCla#194 LHSYSPGBINRVAACLRKLGVPPLRAWRHR CTGCATAGCTATAGCCCTGGCGAAATCAATAGGGTCGCCGCTTGCCTCAGGAAACTGGGAAGTGCCTCCCCTCAGGGCTTGGAGACACAGA

T A R H T P V N S W L G N I I M F A P T L W A R M I L M T H ACCECTAGECATACCCCTGTGAATAGCTGGCTGGGAAACATTATCATGTTCGCTCCCACACTGTGGGCCAGAATGATTCTGATGACCCAT

ENLETT M R S P V P T D N S S P P A V P Q S P Q V A H L GAGAATCTGGAAACCACAATGAGAAGCCCTGTGTTTACCGATAACTCCAGCCCTCCCGCTGTGCCTCAGTCCTTCCAAGTGGCTCACCTC

HepCla #91

A T P P G S V T V P H P N I E E V A L S T T G E I P F Y G K

#### 135/216

GCCACACCCCTGGCTCCGTGACAGTGCCTCACCCTAACATTGAGGAAGTGGCTCTGTCCACCACAGGGGAAATCCCTTTCTATGGCAAA

HepCla #60

LVFDITKLLLAVFGPLNILQASLLKVPYFV CTGGTCTTCGATATCACAAAGCTCCTGCTCGCCGTCTTCGGACCCCTCTGGATTCTGCAAGCCTCCTGCTCAAGGTCCCCTATTTCGTC

TAALV MAQLLRIPQAILD MIAGAH W G V L A G ACCECTGCCCTCGTGATGGCCCAACTGCTCAGGATTCCCCAAGCCATTCTGGATATGATTGCCGGAGCCCATTGGGGAGTGCTCGCCGGA

HepCla #98
C N T C V T Q T V D F S L D P T F T I E T T T L P Q D A V S TGCAATACCTGTGTGACACAGACAGTGGATTTCTCCCTGGATCCCACATTCACAATCGAAACCACAACCCTCCCCCAAGACGCTGTGTCC

H G P T P L L Y R L G A V Q N E V T L T H P V T K Y I M T C CACGGACCCACACCCCTCCTGTATAGGCTCGGCGCTGTGCAAAACGAAGTGACACTGACACACCCTGTGACAAAGTATATCATGACCTGT

ARVAIKS LTERLYVGG PLT NSRGENCGYRR GCCAGAGTGGCTATCAAAAGCCTCACCGAAAGGCTCTACGTCGGCGGACCCCTCACCAATAGCAGAGGCGAAAACTGTGGCTATAGGAGA

HepCla #39

C V I G G A G N N T L H C P T D C P R K H P E A T Y S R C G TGCGTCATCGGAGGCGCTGGCAATAACACTGCATTGCCCTACCGATTGCTTTAGGAAACACCCTGAGGCTACCTATAGCAGATGCGGA

T C G S S D L Y L V T R H A D V I P V R R G D S R G S L L ACCTGTGGCTCCAGGGATCTGTATCTGGTCACCAGACACGCTGACGTCATCCCTGTGAGAAGGAGGCGATAGCAGAGGCTCCCTGCTC

HepCla #138

N M W S G T F P I N A Y T T G P C T P L P A P N Y T F A L W AACATGTGGTCCGGCACATTCCCTATCAATGCCTATACCACAGGCCCTTGCACACCCCTCCCCAATTACACATTCGCTCTGTGG

H S T D A T S I L G I G T V L D Q A E T A G A R L V V L A T CACTCCACCGATGCCACAAGCATTCTGGGAATCGGAACCGTCCTGGATCAGGCTGAGACAGCCGGAGCCAGACTGGTCGTGGTCGCCACA

HepCla #130

Y V P E S D A A A R V T A I L S S L T V T Q L L R R L H Q W TACGTCCCCGAAAGCGATGCCGCTGCCAGAGTGACAGCCATTCTGTCCAGCCTCACCGTCACCCAACTGCTCAGGAGACTGCATCAGTGG

RPSWGPTDPRRRSRNLGKVIDTLTCGFADL AGGCCTAGCTGGGGCCCTACCGATCCCAGAAGGAGAAGCAGAAACCTCGGCAAAGTGATTGACACACTGACATGCGGATTCGCTGACCTC

G P D Q R P Y C W H Y P P K P C G I V P A K S V C G P V Y C 

HepCla #115

B E C S Q H L P Y I E Q G M M L A E Q P K Q K A L G L L Q T GAGGAATGCTCCCAGCATCTGCCTTACATTGAGCAAGGCATGATGCTCGCCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACA

Q A T V C A R A Q A P P P S W D Q M W K C L I R L K P T L TACCAAGCCACAGTGTGTGCCAGAGCCCAAGCCCCTAGCTGGGACCAAATGTGGAAGTGTCTGATTAGGCTCAAGCCTACCCTC

HepCla #34

C G I V P A K S V C G P V Y C P T P S P V V G T T D R S G 

HepCla #131

S S L T V T Q L L R R L H Q W I S S E C T T P C S G S W L R 

D L S D G S W S T V S S E A G T E D V V C C S M S Y S W T G GACCTCAGCGATGGCTCCTGGTCCACCGTCAGCTCCGAGGCTGGCACAGAGGATGTGGTCTGCTGTAGCATGAGCTATAGCTGGACCGGA

HepCla #108

W D Q M W K C L I R L K P T L H G P T P L L Y R L G A V Q N TGGGATCAGATGTGGAAATGCCTCATCAGACTGAAACCCACACTGCATGGCCCTACCCCTCTGCTCTACAGACTGGGAGCCGTCCAGAAT

#### 136/216

HepCla #116

LABQFKQKALGLLQTASRQABVIAPAVOTN CTGGCTGAGCAATTCAAACAGAAAGCCCTCGGCCTCCTGCAAACCGCTAGCAGACAGGCTGAGGTCATCGCTCCCGCTGTGCAAACCAAT

HepCla #118

W Q K L E V F W A K H M W N F I S G I Q Y L A G L S T L P G TGGCAAAAGCTCGAGGTCTTCTGGGCCAAACACATGTGGAATTTCATTAGCGGAATCCAATACCTCGCCGGACTGTCCACCCTCCCCGA

LIAFASRGNHVSPTHYVPESDAAARVTAIL CTGATTGCCTTTGCCTCCAGGGGAAACCATGTGTCCCCCACACACTATGTGCCTGAGTCCGACGCTGCGCTAGGGTCACCGCTATCCTC

HepCla #19

ATLCSALYVGDLCGSVFLVGQLPTFSPRRH GCCACACTGTGTAGCGCTCTGTATGTGGGAGACCTCTGCGGAAGCGTCTTCCTCGTGGGACAGCTCTTCACATTCTCCCCCAGAAGGCAT

HepCla #102

S S V L C E C Y D A G C A W Y E L T P A E T T V R L R A Y M 

GNVAAQLAAPGAATAPVGAGLAGAAIGSVG GGCTGGGTGGCCCAACTGGCTGCCCTGGCGCTGCCACAGCCTTTGTGGGAGCCGGACTGGCTGCCATTGGCTCCGTGGGA

HepCla #29

S W H I N S T A L N C N E S L N T G W L A G L P Y Q H K P N AGCTGGCACATTAACTCCACCGCTCTGAATTGCAATGAGTCCCTGAATACCGGATGGCTCGCCGGACTGTTTTTACCAACACAAATTCAAT

HepCla #164

N A L S N S L L R H H N L V Y S T T S R S A C Q R Q K K V T AACGCTCTGTCCAACTCCCTGCTCAGGCATCACAATCTGGTCTACTCCACCACAAGCAGAAGCGCTTGCCAAAGGCAAAAGAAGTGACA

A A M S T N P K P Q R K T K R N T N R R P Q D V K F P G G G GCCGCTATGTCCACCAATCCCAAACCCCAAAGGAAAACCAAAAGGAATACCAATAGGAGACCCCAAGACGTCAAGTTTCCCGGAGGCGGA

SQTKQSGENFPYLVAYQATVCARAQAPPPS 

A PTYSWGAND TDV PVL NNTRPPLGNW PGCT GCCCCTACCTATAGCTGGGGCGCTAACGATACCGATGTGTTTTGTGCTCAACAATACCAGACCCCCTCTGGGAAACTGGTTCGGATGCACA

HepCla #156

V P P P R K K R T V V L T E S T L S T A L A E L A T K S F G GTGCCTCCCCTAGGAAAAAGGAACCGTCGTCCTCACCGAAAGCACACTGTCCACCGCTCTGGCTGAGCTCGCCACAAAGTCCTTCGGA

S T T S R S A C Q R Q K K V T F D R L Q V L D S H Y Q D V L AGCACAACCTCCAGGTCCGCCTGTCAGAGACAGAAAAAGGTCACCTTTGACAGACTGCAAGTGCTCGACTCCCACTATCAGGATGTGCTC

HepCla #90

D Q A E T A G A R L V V L A T A T P P G S V T V P H P N I E GACCAAGCCGAAACCGCTGGCGCTAGGCTCGTGGTCCTGGCTACCGCTACCCCTCCCGGAAGCGTCACCGTCCCCATCCCAATATCGAA

HepCla #141
PHYVTGMTTDNLKCPCQVPSPBPFTBLDGV TTCCATTACGTCACCGGAATGACAACCGATAACCTCAAGTGTCCCTGTCAGGTCCCCTCCCCCGAATTCTTTACCGAACTGGATGGCGTC

LKLTPIAAAGRLDLSGWFTAGYSGGDIYHS 

A S R Q A E V I A P A V Q T N W Q K L E V P W A K H M W N F GCCTCCAGGCAAGCCGAAGTGATTGCCCCTCCCGTCCAGACAAACTGGCAGAAACTGGAAGTGTTTTTGGGCTAAGCATATGTGGAACTTT

HepCla #181

C R A S G V L T T S C G N T L T C Y I K A R A A C R A A G L 

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HepCla #166

HepCla #180

G P L T N S R G B N C G Y R R C R A S G V L T T S C G N T L GGCCCTCTGACAAACTCCAGGGGAGAAATTGCGGATACAGAAGGTGTAGGGCTAGCGGAGAGTGCTCACCACAAGCTGTGGCAATACCCTC

HepCla #136

IMHTRCHCGAEITGHVKNGTMRIVGPRTCR ATCATGCACACAGGTGTCACTGTGGCGCTGAGATTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGCAGA

HepCla #144

EVSPRVGLHBYPVGSQLPCEPPPDVAVLTS
GAGGTCAGCTTTAGGGTCGGCCTCCACGAATACCCTGTGGGAAGCCAACTGCCTTGCGAACCCGAACCCGATGTGCTGCTCACCTCC

HepCla #167

KEVKAAASKVKANLLSVEEACSLTPPHSAK

HepCla #59

G R D A V I L L M C V V H P T L V P D I T K L L L A V F G P GGCAGAGACGCTGGGTTCTGGCTGTGTGGCCCCTACCCTGGTGTTTGACATTACCAAACTGCTCCTGGCTGTTTTGGCCCT

HepCla #146

HepCla #78

S P R P I S Y L K G S S G G P L L C P A G H A V G I F R A A AGCCCTAGGCCTATCTCCTAAGGGAAGCTCCGGGGGACCCCTCCTGTGTCCCGCTGGCCATGCCGTCGGCATTTTCAGAGCCGCT

HepCla #32

D P D Q G W G P I S Y A N G S G P D Q R P Y C W H Y P P K P GACTITGACCAAGGCTGGGGCCCTATCCCCCTAAGGCGGAGCCGATCAGAGACCCTATTGCTGGCACTATCCCCCTAAGGCT

HepCla #128

HepCla #50

C L W M M L L I S Q A B A A L B N L V I L N A A S L A' G T H
TGCCTCTGGATGATGCTCCTCATTAGCCCAGCCCGAAGCCCCAT

HepCla #114

I I P D R E V L Y R E P D E M E E C S Q H L P Y I E Q G M M ATCATTCCCGATAGGGAAGTGCTCTACAGAGAGTTTGACGAAATGGAAGTGTTAGCCAACACCTCCCCTATATCGAACAGGGAATGATG

HepCla #47

L I H L H Q N I V D V Q Y L Y G V G S S I A S W A I K W E Y CTGATTCACCTCCACCAAAACATTGTGGATGTGCAATACCTCTACGGAGGTGGGAAGCTCCATCGCTGGGCCCATTAAGTGGGAGTAT

HepCla #200

V S H A R P R W P W P C L L L A A G V G I Y L L P N R A A GTGTCCCACGCTAGGCGTAGGTGGTTCTGGTTCTGCTCCTGCTCGCCGCTGGCGTTGGCATTTACCTCCTGCTAACAGAGCCGCT

RepCla #85

A A T L G P G A Y M S K A H G I D P N I R T G V R T I T T G GCCGCTACCCTCGGCTTTGGCGCTTACATCACAAGCCCATGGCATTGACCCTAACATTAGGACAGGCGTCAGGACAATCACAACCGGA

HepCla #62

R V Q G L L R I C A L A R K M I G G H Y V Q M A I I K L G A AGGGTCCAGGGACTGCTCAGGATTGCGCTCTGGCTAGGAAATGATTGGCGGACACTATGTGCAAATGGCTATCATTAAGCTCGGCGCT

HepCla #153

RRPAQALPVWARPDYNPPLVBTWKKPDYBPAGGAGATTCGCTCAGGCTCTGGCTGACTATGAGCCT

HepCla #72

T A A Q T P L A T C I N G V C W T V Y H G A G T R T I A S P ACCECTECCCAAACCTTTCTGGCTACCATGGCGTCTGCCCTTACCATGGCGCTCTGCCCCTACCATGGCGCTCGCCCAAACCTTTCTGGCTATCAATGGCGCTCTGCCCCTTACCATGGCGCTCTGCCACAAGGACAATCGCTTACCCTT

HepCla #65

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WAHNGLRDLAVAVEPVVPSQMETKLITWGATGGCCTCAGAGGCCTCAGAATGGCCTCAGAGGCCTCTGGCTGTGGAACCCAAATGGCAAACGAAACGAAACTGATTACCTGGGGCGCT

HepCla #74

K G P V I Q M Y T N V D Q D L V G W P A P Q G S R S L T P C AAGGGACCCGTCATCAAATGTATACCAATGTGGATCAGGATCTGGTCGGCTGGCCCGCTCCCCAAGGCTCCAGGTCCCTGACACCCTGT

HepCla #151

KVVILDSPDPLVABBDBRBISVPABILRKS

HepCla #64

LTGTYVYNHLTPLRDWAHNGLRDLAVAVEPCTGACAGGCACATAACGGACACTCACCCTCACCCCTCGAGAGACTGGGCCCATAACGGACTGAGAGACCTCGCCGTCGCCGTCGAGGCCT

HepCla #80

V C T R G V A K A V D P I P V B N L B T T M R S P V F T D N
GTGTGTACCAGAGGCGTCGCCAAAGCCGTCGACTTTACCAGACAAT

HenCla figs

A L G I N A V A Y Y R G L D V S V I P T S G D V V V V A T D GCCCTCGGCATTAACGCTGTCGTCATACGCGATTCCCACAAGCGGAGACGTCGTGGTCGTGGCTACCGAT

HepCla #111

HepCla #97

A L M T G Y T G D F D S V I D C N T C V T Q T V D F S L D P GCCCTCATGACAGGCTATACCGGGAGACTTTGACTCCGTGATTGACTGTTAACACATGCGTCACCCAAACCGTCGACTTTAGCCTCGACCCT

HepCla #2

N T N R R P Q D V K P P G G G Q I V G G V Y L L P R R G P R AACACAAACAGAAGGCCTCAGGATGTGAAATTCCCTGGCGGAGGCCAAATCGTCGCCGGAGGCGACTCTATCTCCTCCCCAGAAGGGGACCCAGA

HepCla #11

RALAHGVRVLBDGVNYATGNLPGCSPSIPLAGGGCTCTGGCTCAGGAGTGCCTCAGGATGCCTCAGGATGCCTCAGGATGCCTCAGCATTTCCTC

HepCla #169

S K P G Y G A K D V R C H A R K A V A H I N S V W K D L L R AGCAAATTCGGATACGGAGCCAAAGACGTCAGGGTGTCACGCTAGGAAAGCCCTCCTGGAA

HepCla #28

T P G A K Q N I Q L I N T N G S N H I N S T A L N C N E S L ACCCCTGGCGCTAAGCAAAACATTCAGCTCATCAATACCAATGCTCCTGGCATATCAATAGCACAGCCCTCAACTGTAACGAAAGCCTC

HepCla #30

N T G W L A G L P Y Q H K P N S S G C P E R L A S C R R L T AACACAGGCTGGCTGGCTGTCTTCTATCAGCATAAGTTTAACTCCAGCGGATGCCCTGAGAGACTGGCTAGCTGTAGGAGACTGACA

HepCla #49

V V L L P L L A D A R V C S C L N M M L L I S Q A E A A L GTGGTCCTGCTCGTCGCTGGCTGAGGCTGAGGCTGCCCTC

HepCla #192

D C E I Y G A C Y S I E P L D L P P I I Q R L H G L S A F S GACTGTGAGATTTACGGAGCCTGTTACTCCATCGAACCCCCCGACCTCCCCCCTATCATCAGAGACTGCATGGCCTCAGCGCTTTCTCC

HenCla #77

W T V Y H G A G T R T I A S P K G P V I Q M Y T N V D Q D L
TGGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCCAAAGGCCCTGTGATTCAGATGTACACAAACGTCGACCAAGACCTC

HepCla #101

Y R P V A P G E R P S G M P D S S V L C E C Y D A G C A W Y TACAGATTCGTCGCCCCTGGCGAAAGGCCTTACCGATGTTTGACTCCAGCGTCCTGTTGTACTGCATGCCGGATGCCCTTGGTAT

HeoCla #45

R S B L S P L L S T T Q W Q V L P C S P T T L P A L S T G
AGGTCCGAGCTCAGCCCTCTGCTCCACCACAGAGTGGCAGGTCCTGCCTCGCTTCACAACCCTCCCCGCTCTGTCCACCGGA

HepCla #195

LRKLGVPPLRAWRHRARSVRARLLARGGRA

#### 139/216

 $\tt CTGAGAAAGCTCGGCGTCCCCCTCTGAGAGCCTGGAGGCCATAGGGCTAGGTCCGTGAGAGCCAGACTGCTCGCCAGAGGCCGAAGGGCT$ 

HepCla #121

HepCla #61

L W I L Q A S L L K V P Y F V R V Q G L L R I C A L A R K M CTGTGGATCCTCCAGGCTAGCCTCCTGAAAGTGCCTTACTTTGTGAGAGTGCAGAGCCTCCTGAGAATCTGTGCCCTCGCCAGAAAGATG

HepCla #137

V K N G T M R I V G P R T C R N M W S G T F P I N A Y T T G GTGAAAAACGGAACCATGAGGATTGTGGGACCCAGAACCTGTAGGAATATGTGGAGCGGAACCTTTCCCATTAACGCTTACACAACCGGA

HepCla #92

EVALSTTGBIPFYGKAIPLEVIKGGRAGGCAGACACCTCATCTTT

HepCla #188

L T R D P T T P L A R A A W E T A R H T P V N S W L G N I I CTGACAAGGGATCCCACAACCCCTCTAGGCTAGGGCTGCCTGGGAGACACCACACACCCCGTCAACTCCTGGCTAGGCAATATCATT

HepCla #14(

R V S A E B Y V E I R R V G D F H Y V T G M T T D N L K C P AGGGTCAGCGCTGAGGATACGTCGAGATTAGGAGAGTGGGGAGACTTTCACTATGTGACAGGCATGACCACAGACAATCTGAAATGCCCT

HepCla #155

PVVHGCPLPPPRSPPVPPPRKKRTVVLTES

HepCla #157

T L S T A L A E L A T K S F G S S S T S G I T G D N T T T S ACCCTCAGCACAGCCCTCGCCAAACTGCCTACCAAAAGCTTTGGCTCCAGCTCCACCTCCGGCATTACCGGAGACAATACCACAACCTCC

HepCla #135

V S C Q R G Y K G V W R G D G I M H T R C H C G A E I T G H GTGTCCTGCCAAAGGGGATACAAGGCGTCTGGAGAGGCGATTGCGATGCCATTGCGGAGCCGAAATCACAGGCCAT

HepCla #20

V P L V G Q L P T F S P R R H W T T Q G C N C S I Y P G H I GTGTTTCTGGTCGGCCAACTGTTTACCCTTAGGAGACACTGGACCACAGGGATGCAATTGCTCCATCTATCCCGGACACATT

HepCla #123

PVGAGLAGATIGSVGLGKVLVDILAGYGAG TTCGTCGCCGCCTCGCCGCGCCTCCGCCAACTCCTCGCCAACTCCTCGCCGGATACCGCACCCGGA

HepCla #133

D I W D W I C B V L S D P K T W L K A K L M P Q L P G I P P GACATTTGGGATTGGGAAGTGCTGGGAAGTGCTGGCATTCCCTTT

HepCla #15

N S S I V Y B A A D A I L H T P G C V P C V R E G N A S R C AACTCCAGCATTGTGTATGAGGCTGCCGATGCCTTCGCATACCCCTGGCTGTGTGCCTTAGGGAAGGCAATGCCTCCAGGTGT

HeoCla #31

SSGCPERLASCRRLTDPDQGWGPISYANGSAGCTCCCGCTGTCCCGAAAGGCTCCCGAAAGGCTCCCGAAAGGCTCCCCAGAAGGCTCACCGATTTCGATCAGGGATGGGGACCCATTAGCTATGCCAATGGCTCC

HepCla #178

RTEBAIYQCCDLDPQARVAIKSLTBRLYVG AGGACAGAGGAAGCCATTTACCAATGCTGTGACCTCGACCCTCAGGCTAGGCTCGCCATTAAGTCCCTGACAGAGAGACTGTATGTGGGA

HepCla #69

V S K G W R L L A P I T A Y A Q Q T R G L L G C I I T S L T GTGTCCAAGGGACATGCTCGGCTGTTCCCTTACCACCACACAGGGGACTGCTCGGCTGTTCCTCCCTGACA

HepCla #191

F P S V L I A R D Q L B Q A L D C E I Y G A C Y S I E P L D TTCTTTAGCGTCCTGATTGCCACGAGCCCACTGGAACAGGCTCTGGATTGCGAAATCTATGCGCTTGTATAGCATTGAGCCTCTGGAT

HepCla #142

C Q V P S P E P F T E L D G V R L H R F A P P C K P L L R E TGCCAAGTGCCTAGCCCTGAGGGTTTTTCACAGAGCTCGACGGAGTGAGACTGCATAGGTTTTGCCCCTCCTGTAAGCCTCTGCTCAGGGAA

# 140/216

HepCla #182

TCYIKARAACRAAGLQDCTMLVCGDDLVVI ACCTGTTACATTAAGGCTAGGGCTGCCGTAGGGCTGCCGGACTGCAAGACTGTACCATGCTGGTCTGCGGGAGACGATCTGGTCGTGATT

I D P N I R T G V R T I T T G S P I T Y S T Y G K P L A D G ATCGATCCCAATATCAGAACCGGAGTGAGAACCATTACCACAGGCTCCCCCATTACCTATAGCACATACGGAAAGTTTCTGGCTGACGGA

HepCla #44

C N W T R G B R C D L E D R D R S E L S P L L L S T T Q W Q 

HepCla #22

T G H R N A W D M M M N W S P T A A L V M A Q L L R I P Q A ACCGGACACAGAATGGCTTGGGATATGATGAATTGGTCCCCCACAGCCGCTCTGGTCATGGCTCAGCTCCTGAGAATCCCTCAGGCT

HepCla #127

P G A L V V G V V C A A I L R R H V G P G B G A V Q W M N R CCCGGAGCCCTCGTCGTCGCCGTGTGTGCCCCCTATCCTCAGGAGACACGTCGCCCTGGCCGAGGCGCTGTGCAATGGATGAACAGA

H D S P D A E L I E A N L L W R Q E M G G N I T R V E S E N CACGATAGCCCTGACGCTGAGCTCATCGAAGCCAATCTGCTCTGGAGACAGGAAATGGGAGGCAATATCACAAGGGTCGAGTCCGAGAAT

HepCla #105

B G V F T G L T H I D A H F L S Q T K Q S G E N F P Y L V A GAGGGAGTGTTTACCGGACAGACACACTTGACGCTCACTTTCTGTCCCAGACAAAGCGAAAGCGAGAGAATTTCCCTTACCTCGTGGCT

RGRRQPIPKARRPEGRTWAQPGYPWPLYGN AGGGGAAGGACAGCCTATCCCTAAGGCTAGGAGACCCGAAGGCAGAACCTGGGCCCAACCCGGATACCCTTGGCCTCTGTATGGCAAT

LIVPPDLGVRVCEKMALYDVVSKLPLAVMG 

HepCla #12

Y AT GNLPGCS FSIPLLALLS CLT V PASAY Q TACGCTACCGGAAACCTCCCGGATGCTCCTTCTCCATCTTTCTGCTCGCCTCCTGTCCTGCCTCACCGTCCCCGCTAGCGCTTACCAA

HepCla #124

LGKVLVDILAGYGAGVAGALVAFKIMSGRV CTGGGAAAGGTCCTGGTCGACATTCTGGCTGGCTATGGCGCTCGCCGCGAGCCCTCGTGGCTTTCAAAATCATGAGCGGAGAGGTC

HepCla #160

S Y S S M P P L B G B P G D P D L S D G S W S T V S S E A G AGCTATAGCTCCATGCCTCCCTCGAGGGAGAGCCTGGCGATCCCGATCTGTCCGACGGAAGCTGGAGCACAGTGTCCAGCGAAGCCGA

RQEMGGNITRVESENKVVILDSFDPLVAEE AGGCAAGAGATGGGCGGAAACATTACCAGAGTGGAAAGCGAAAACAAAGTGGTCATCCTCGACTCCTTCGATCCCTCGTGGCTGAGGAA

HepCla #75
V G W P A P Q G S R S L T P C T C G S S D L Y L V T R H A D GTGGGATGGCCTGCCCTCAGGGAAGCAGAAGCCTCACCCCTTGCACATGCGGAAGCTCCGACCTCTACCTCGTGACAAGGCATGCCGAT

G C S G G A Y D I I I C D E C H S T D A T S I L G I G T V L GGCTGTAGCGGAGGCGCTTACGATATCATTATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCGGCATTGGCACAGTGCTC

T F T I B T T T L P Q D A V S R T Q R R G R T G R G K P G I ACCTITACCATTGAGACAACCACACTGCCTCAGGATGCCGTCAGCAGAACCCAAAGGAGAGGCAGAACCGGAAGGGGAAAGCCTTGGCATT

HepCla #40
D C P R K H P E A T Y S R C G S G P W I T P R C L V D Y P Y GACTGTTTCAGAAAGCATCCCGAAGCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTGGTCGACTATCCCTAT

HepCla #201

LAAGVGIYLLPNRAA CTGGCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCC

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HepCla #163

ALVTPCAAEEQKLPINALSNSLLRHHNLVY GCCCTCGTGACACCCTGTGCCGCAGAACAGGAACACGAAACCTCGTGTAT

HepCla #132

I S S B C T T P C S G S W L R D I W D W I C E V L S D F K T ATCTCCAGCGAATGCACACCCCTTGCTCCGGCTCCTGGCTCAGGGATTCTGGGACTGGTCTGTGAGGTCCTGTCCGACTTTAAGACA

HepCla #134

WLKAKLMPQLPGIPPVSCQRGYKGVWRGDG
TGGCTCAAGGCTAAGCTCATCCTCAGCTCCCCGGAATCCCTTTCGTCAGCTGTCAGAGAGGCTATAAGGGAGTGTGGAGGGGAGACGGA

HepC1a #41

S G P W I T P R C L V D Y P Y R L W H Y P C T I N Y T I F K
AGCGGACCCTGGATCACACTGAGACTGCCTTACAGACTGTGGCACTATCCCTTACCATTAACTATACCATTTCAAA

#### Artificial Protein:

vipvrrgdsrgsllsprpisylkgssggparrgreiligpadgmvskgwrllapitayarlhrfappckpllreevsprvglheypvgsvvpsomet KLITWGADTAACGDIINGLPVSLLCPAGHAVGIFRAAVCTRGVAKAVDFIFVCVVIVGRIVLSGKPAIIPDREVLYREFDEMPCTPLPAPNYTFALWR vsabeyveirrvgdalydvvsklplavwgssygfqyspgqrvefiswclwwlqyfltrvbaqlhvwvpplnvrgenlvilnaaslagthglvsflvff CFAWYLLPPIIQRLHGLSAFSLHSYSPGBINRVAACNPPLVETWKKPDYEPPVVHGCPLPPPRSPPGVGSSIASWAIKWBYVVLLFLLLADARVCSLN ntrpplgnnfgctwinstgftkvcgappfteawtrysappgdppqpbydlblitscsswpllllllalpqrayaldtevaascggvvlqqtrgllgci ITSLTGRDKNQVEGEVQIVSSSPPAVPQSFQVAHLHAPTGSGKSTKVPAANTPGLPVCQDHLEFWEGVFTGLTHIDAHFLVLLLPAGVDAETHVTGGN agrttsglvsllevtlthpvtkyimtcmsadlevvtstwvlvvglmaltlspyykryiswclmnlqyfltrvaicgkylpnmavrtklkltpiaaagr LDLSIAYFSMVGNWAKVLVVLLLFAGVDAETHVTRLARGSPPSMASSSASQLSAPSLKATCTANGLVSPLVPFCFAWYLKGRWVPGAVYALYGMOLPC EPEPDVAVLTSMLTDPSH1TABAAGRDSVTP1DTT1MAKNEVFCVQPEKGGRKPARYAAQGYKVLVLNPSVAATLGFGAYMSKAHGVRNSTGLYHVTN DCPNSSIVYEAADAILHTSSYGPQYSPGQRVEFLVQAWKSKKTPMGFSDTAACGDIINGLPVSARRGREILLGPADGMSQLSAPSLKATCTANHDSPD ablibanllwnpaiaslmaftaavtsplitsqtllpniiglvqawkskktpmgfsydtrcfdstvtesdiderbisvpabilrksrrpaqalpvwarp DYMPAPTLNARMILMTHFPSVLIARDQLEQALSVIPTSGDVVVVATDALMTGYTGDFDSVIDCHSKKKCDELAAKLVALGINAVAYYRGLDVVLPCSF TTLPALSTGLIHLHQNIVDVQYLYKGRWVPGAVYALYGMWPLLLLLLALPQRAYSPITYSTYGKFLADGGCSGGAYDIIICDBCARSVRARLLARGGR aaicgkylfnwavrtkkavahinsvwkdlledsvtpidttimakneptpspvvvgttdrsgaptyswgandtdvfvpgcvpcvregnasrcwvamtpt vatrdgklqdctmlvcgddlvvicesagvqedaaslravagalvafkimsgevpstedlvnllpailsydtrcfdstvtesdirtbeaiyqccdldpq eltpaettvrlraymytpglpvcqdhlefwpqpeydlelitscssnvsvahdgagkrvyylgkvidtltcgpadlmgyiplvgaplggaaaiplevik ggrhlifchskkkcdelaaklvggvlaalaayclstgcvvivgrivlsgkpacesagvqedaaslrafteamtrysappgdpgwftagysggdiyhsv SHARPRWFWPCLLLSSSTSGITGDNTTTSSEPAPSGCPPDSDAERTQRRGRTGRGKPGIYRFVAPGERPSGMFDVRMYVGGVEHRLEAACNWTRGERCdledrdeaqlhvwvpplnvrggrdavillmcvvhptlgvratrktsersqprgrrqpipkarrpegnvsvahdgagkrvyyltrdpttplaraawese PAPSGCPPDSDAESYSSMPPLEGEPGDPIGGHYVQMAIIKLGALTGTYVYNHLTPLRDPSTEDLVNLLPAILSPGALVVGVVCAAILRILDMIAGAHW GVLAGIAYFSMVGNWAKVLVEGCGWAGWLLSPRGSRPSWGPTDPRRRSRNWTTQGCNCSIYPGHITGHRMAWDMMNWSPWVAMTPTVATRDGKLPAT QLRRHIDLLVGSRLWHYPCTINYTIPKVRMYVGGVEHRLEAAVFCVQPEKGGRKPARLIVFPDLGVRVCEKMMGYIPLVGAPLGGAARALAHGVRVLE DGVNGGNAGRITSGLVSLLTPGAKQNIQLINTNGLALLSCLTVPASAYQVRNSTGLYHVTNDCPGRDKNQVEGEVQIVSTAAQTFLATCINGVCPATO LRRHIDLLVGSATLCSALYVGDLCGSHAPTGSGKSTKVPAAYAAQGYKVLVLNPSVRTWAQPGYPWPLYGNEGCGWAGWLLSPRGSTEDVVCCSMSYS wtgalvtpcaaeeqklp1aldtevaascggvvlvglmaltlspyykrywmnstgftkvcgappcv1ggagnntlhcptsveeac5ltpphsakskfgy gakdvrcharisgiqylaglstlpgnpaiasimaptaavtqivggvyllprrgprlgvratrktsersqplhsyspgbinrvaaclrklgvpplrawr HRTARHTPVNSWLGNIIMPAPTLWARMILMTHENLETTMRSPVFTDNSSPPAVPQSFQVAHLATPPGSVTVPHPNIEEVALSTTGBIPFYGKLVFDIT KLLLAVFGPLNILQASLLKVPYFVTAALVMAQLLRIPQAILDMIAGAHNGVLAGCNTCVTQTVDFSLDPTFTIETTTLPQDAVSHGPTPLLYRLGAVO nevtlthpvtkyimicarvaikslterlyvggplinsrgencgyrrcviggagnntlhcptdcfrkhpbatysrcgtcgssdlylvtrhadvipvrrr GDSRGSLLNMNSGTFPINAYTTGPCTPLPAPNYTFALMHSTDATSILGIGTVLDQAETAGARLVVLATYVPESDAAARVTAILSSLTVTOLLRRLHOW RPSWGPTDPRRRSRNLGKVIDTLTCGFADLGPDQRPYCWHYPPKPCGIVPAKSVCGPVYCEECSQHLPYIEQGWMLAEQFKQKALGLLQTYQATVCAR AQAPPPSWDQMWKCLIRLKPTLCGIVPAKSVCGPVYCPTPSPVVVGTTDRSGSSLTVTQLLRRLHQWISSECTTPCSGSWLRDLSDGSWSTVSSEAGT edvvccsmsyswtgwdqwwkclirlkptligptpllyrigavqnlaeqpkqkalgllqtasrqaeviapavqtnwqklevfwakhwwnfisgiqylag LSTLPGLIAFASRGNHVSPTHYVPBSDAAARVTAILATLCSALYVGDLCGSVFLVGQLPTFSPRRHSSVLCECYDAGCAWYELTPAETTVRLRAYMGW vaaqlaapgaatafvgaglagaaigsvgswhinstalncneslntgwlaglfyqhkfnnalsnsllrhhnlvysttsrsacorokkytaamstnpkpo RKTKRNTNRRPQDVKPPGGGSQTKQSGENPPYLVAYQATVCARAQAPPPSAPTYSMGANDTDVFVLNNTRPPLGNNFGCTVPPPRKKRTVVLTESTLS TALABLATKSFGSTTSRSACQRQKKVTFDRLQVLDSHYQDVLDQAETAGARLVVLATATPPGSVTVPHPN1EFHYVTGMTTDNLKCPCOVPSPEFFTE LDGVLKLTPIAAAGRLDLSGWPTAGYSGGDIYHSASRQAEVIAPAVQTNNQKLEVFWAKHWWNFCRASGVLTTSCGWTLTCYIKARAACRAAGLFDRL  ${\tt QVLDSHYQDVLKEVKAAASKVKANLLGPLINSRGENCGYRRCRASGVLTTSCGNTLINHTRCHCGABITGHVKNGTMRIVGPRTCREVSFRVGLHEYP}$ vgsqlpcepepdvavltskevkaaaskvkanllsvebacsltpphsakgrdavillmcvvhptlvfditklllavfgpmltdpshitaraagrrlarg SPPSMASSSAS PRPISYLKGSSGGPLLCPAGHAVGI PRAADPDQGWGPI SYANGSGPDQRPYCWHYPPKPRIIVGPGEGAVOWMIRLI APASRGNHVS P THCLMMMLLISQABAALENLVILNAASLAGTHIIPDRBVLYRBPDEMBECSQHLPYIBQGMMLIHLHQNIVDVQYLYGVGSSIASWAIKWBYVSHARP rwfwpcllllaagvgiyllpnraaaatigpgaymskahgidpnirtgvrtittgrvqgllricalarkmigghyvqmaiiklgarrpaqalpvwarpd YNPPLVETWKKPDYEPTAAQTFLATCINGVCWTVYHGAGTRTIAS PWAHNGLRDLAVAVEPVVFSQMETKLITWGAKGPVIQMYTNVDQDLVGWPAPQ gsrsltpckvvillospdplvaeedereisvpabilrksltgtyvynhltplrdwahnglrdlavavepvctrgvakavdpipvehlettmrspvptdn  $\textbf{ALGINAVAYYRGLDVSVIPTSGDVVVVATDMSADLBVVTSTWVLVGGVLAALAAYCLSTGALMTGYTGDFDSVIDCNTCVTQTVDFSLDFMTMRRPQD$ vkppgggqivggvyllprrgprralahgvrvledgvnyatgnlpgcspsiplskfgygakdvrcharkavahinsvnkdlletpgakqniqlintngs whinstalncneslntgnlaglpyqhkpnssgcperlascrrltvvllpllladarvcsclmmillisqaeaaloceiygacysieplolppiiqrlh GLSAFSWTVYHGAGTRTIASPRGPVIQMYTNVDQDLYRPVAPGERPSGMFDSSVLCECYDAGCAWYRSELSPLLLSTTQMOVLPCSFTTLPALSTGLR klgvpplrawrhrarsvrarilarggrasplttsqtllfnilggwvaaqlaapgaatalnilqasilkvpyfvrvqgllricalarkmvxxstmrivg prtcrnmnsgtppinayttgevalstigeippygkaiplevikggrhlifltrdpttplaraanetarhtpvnswlgniirvsaeeyveirrvgdphy vtcmttdnlkcppvvhgcplppprsppvppprkkrtvvltestlstalablatkspgssstsg1tgdntttsvscqrgykgvmrgdg1mhtrchcgae ITGHVPLVGQLPTPSPRRHWTTQGCNCSIYPGHIPVGAGLAGAAIGSVGLGKVLVDILAGYGAGDIWDWICEVLSDPKTWLKAKLMPOLPGIPFNSSI vybaadailhtpgcvpcvregnasrcssgcperlascrrltdpdgwgpisyangsrteeaiyqccdldpqarvaikslterlyvgvskgwrllapit AYAQQTRGLLGCIITSLTPFSVLIARDQLEQALDCEIYGACYSIBPLDCQVPSPEPFTELDGVRLHRFAPPCKPLLRETCYIKARAACRAAGLQDCTM

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LVCGDDLVVIIDPNIRTGVRTITTGSPITYSTYGKFLADGCNWTRGERCDLEDRDRSELSPLLLSTTQWQTGHRMAWDMMNWSPTAALVMAQLLRIP QAPGALVVGVVCAAILRRHVGPGEGAVQWMNRHDSPDAELIEANLLNRQEMGGNITRVESENEGVFTGLTHIDAHFLSQTKQSGENFPYLVARGRRQP IPKARRPEGRTWAQPGYPWPLYGNLIVPPDLGVRVCEKMALYDVVSKLPLAVMGYATGNLPGCSFSIFLLALLSCLTVPASAYQLGKVLVDILAGYGA GVAGALVAPKIMSGEVSYSSMPPLEGEPGDPDLSDGSWSTVSSEAGRQEMGGNITRVESENKVVILDSPDPLVAEEVGWPAPQGSRSLTPCTCGSSDL YLVTRHADGCSGGAYDIIICDECHSTDATSILGIGTVLTPTIETTTLPQDAVSRTQRRGRTGRGKPGIDCFRKHPEATYSRCGSGPWITPRCLVDYPY PY LAAGVGIYLLPNRAAALVTPCAAEEQKLPINALSNSLLRHHNLVYISSECTTPCSGSWLRDIWDWICEVLSDPKTWLKAKLMPQLPGIPFVSCQRGYK GVWRGDGSGPWITPRCLVDYPYRLMHYPCTINYTIFK

#### Artificial DNA:

GTGATTCCCGTCAGGAGAGGGGGAGACTCCAGGGGGAAGCCTCCTGTCCCCCAGACCCATTAGCTATCTGAAAGGCTCCAGCGGAGGCCCTGCCAGAAG GGGAAGGGAAATCCTCCTGGGACCCGCTGACGGAATGGTCAGCAAAGGCTGGAGGCTCCTGGCTCCCATTACCGCTTACGCTAGGCTCCACAGATTCG CTCCCCCTTGCAAACCCCTCCTGAGAGAGGGAAGTGTCCTTCAGAGTGGGACTGCATGAGTATCCCGTCGGCTCCGTGGTCTTCTCCCAGATGGAGACA AAGCTCATCACATGGGGAGCCGATACCGCTGCCTGTGGGGATATCATTAACGGACTGCCTGTGTCCCTGCCCTGCCCGGACACGCTGTGGGGAAT CITTAGGGCTGCCGTCTGCACAAGGGGAGTGGCTAAGGCTGTGGATTTCATTCCCGTCTGCGTCGTGATTGTGGGAAGGATTGTGCTCAGCGGAAAGC GTGTCCGCCGAAGAGTATGTGGAAATCAGAAGGGTCGGCGATGCCCTCTACGATGTGGTCAGCAAACTGCCTCTGGCTGTGATGGGCTCCAGCTATGG CTTTCAGTATAGCCCTGGCCAAAGGGTCGAGTTTATCTCCTGGTGTCTGTGGTGGTCCAGTATTTCCTCACCAGAGTGGAAGCCCAACTGCATGTGT TGCTTTGCCTGGTACCTCCCGCTTCCCATTATCCAAAGGCTCCACGGACTGTCCGCCTTTAGCCTCCACTCCTACTCCCCCGGAGAGATTAACAGAGT GGCTGCCTGTAACCCTCCCCTCGTGGAAACCTGGAAGAACCCGATTACGAACCCCCTGTGGTCCACGGATGCCCTCTGCCTCCCCCTAGGTCCCCCC  $\tt CTGGCGTCGGCTCCAGCATTGCCTCCTGGGCTATCAAATGGGAATACGTCGTGCTCCTGGTTTCTGCTCCTGGCTGACGCTAGGGTCTGCTCCCTGAAT$ AACACAAGGCCTCCCCTCGGCAATTGGTTTGGCTGTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCTTTCACAGAGGCTAT GACAAGGTATAGCGCTCCCCTGGCGATCCCCCTCAGCCTGAGTATGACCTCGAGCTCATCACAAGCTGTAGCTCCTGGCCTCTGCTCCTGCTCCTGC TCGCCCTCCCCCAAAGGGCTTACGCTCTGGATACCGAAGTGGCTGCCTCCTGCGGAGGCGTCGTGCTCCAGCAAACCAGAGGCCTCCTGGGATGCATT GGTCGTGACAAGCACATGGGTCCTGGTGGGACTGATGGCCCTCACCCTCAGCCCTTACTATAAGAGATACATTAGCTGGTGGCTCTGGTGGCTGC AATACTTTCTGACAAGGGTCGCCATTTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAAGCTCAAGCTCACCCCTATCGCTGCCGCTGGCAGA CTGGATCTGTCCATCGCTTACTTTAGCATGGTGGGAAACTGGGCCAAAGTGCTCGTGGTCCTGCTCCTGTTTGCCGGAGTGGATGCCGAAACCCATGT GACAAGGCTCGCCAGAGGCTCCCCCCTAGCATGGCCTCCAGCTCCGCCTCCCAGCTCAGCGCTCCCTCGAAAGCCACATGCACAGCCAATGGCC TCGTGTCCTTCCTCGTGTTTTTCTGTTTCGCTTGGTATCTGAAAGGCAGATGGGTCCCCGGAGCCGTCTACGCTCTGTATGGCATGCAGCTCCCCTGT GAGCCTGAGCCTGACGTCGCCGTCCTGACAAGCATGCTGACAGACCCTAGCCATATCACAGCCGAAGCCGCTGGCAGAGACTCCGTGACACCCCATTGA CACAACCATTATGGCTAAGAATGAGGTCTTCTGTGCGAACCCGAAAAGGGGAGGCAGAAAGCCTGCCAGATACGCTGCCCAAGGCTATAAGGTCCTGG TCCTGAATCCCTCCGTGGCTGCCACACTGGGATTCGGAGCCTATATGTCCAAGGCTCACGGAGTGAGAAACTCCACCGGACTGTATCACGTCACCGAAT GACTETCCCAATAGCTCCATCGTCTACGAAGCCGCTGACGCTATCCTCCACACAAGCTCCTACGGATTCCAATACTCCCCCGGACAGAGAGTGGAATT CCTCGTGCAAGCCTGGAAGTCCAAGAAAACCCCTATGGGATTCTCCGACACAGCCGCTTGCGGAGACATTATCAATGGCCTCCCCGTCAGCGCTAGGA GAGGCAGAGATTCTGCTCGGCCCTGCCGATGGCCATGAGCCAACTGTCCGCCCCTAGCCTCAAGGCTACCTGTACCGCTAACCATGACTCCCCCGAT GCCGAACTGATTGAGGCTAACCTCCTGTGGAACCCTGCCATTGCCTCCCTGATGGCCTTTACCGCTGCCGTCACCTCCCCCCTCACCACAAGCCAAAC CCTCCTGTTTAACATTCTGGGACTGGTCCAGGCTTGGAAAAGCAAAAAGACACCCATGGGCTTTAGCTATGACACAAGGTGTTTCGATAGCACAGTGA CACTATATGTTTGCCCCTACCCTCTGGGCTAGGATGATCCTCATGACACACTTTTTCTCCGTGCTCATCGCTAGGGATCAGCTCGAGCCAAGCCCCTCAG CGTCATCCCTACCTCCGGCGATGTGGTCGTCGCCACAGACGCTCTGATGACCGGATACACAGGCGATTTCGATAGCGTCATCGATTGCCATAGCA AAAAGAAATGCGATGAGCTCGCCGCTAAGCTCGTGGCTCTGGGAATCAATGCCGTCGCCTATTACAGAGGCCTCGACGTCGTGCTCCCCTGTAGCTTT GTATECCCTCTACGGAATGTGGCCCCTCCTGCTCCTGCTCCTGCCTCAGAGAGCCTATAGCCCTATCACATACTCCACCTATGGCAAATTCC TUGCUGATGGCGGATGCTCCGGCGGAGCCTATGACATTATCATTTGCGATGAGTGTGCCAGAAGCGTCAGGGCTAGGGCTAGGGGAGGCAGA GCCGCTATCTGTGGCAAATACCTCTTCAATTGGGCTGTGAGAACCAAAAAGGCTGTGGCTCACATTAACTCCGTGTGGAAGGATCTGCTCGAGGATAG CGTCACCCCTATCGATACCACAATCATGGCCCAAAAACGAATTCACACCCTCCCCCGTCGTCGCCACAACCGATAGGTCCGGCGCCTCCCACATACT CCTGGGGAGCCAATGACACAGACGTCTTCGTCCCCGGATGCGTCCCCTGTGTGAGAGGGGAAACGCTAGCAGATGCTGGGTGGCTATGACACCCACA GAGCTCACCCCTGCCGAAACCACAGTGAGACTGAGAGCCTATATGAATACCCCTGGCCTCCCCGTCTGCCAAGACCATCTGGAATTCTGGCCCCAACC CGAATACGATCTGGAACTGATTACCTCCTGCTCCAGCAATGTGTCCGTGGCTCACGATGGCGCTGGCAAAAGGGTCTACTACTATCTGGGAAAGGTCATCG ATACCCTCACCTGTGGCTTTGCCGATCTGATGGGCTATATCCCTCTGGTCGGCGGTCCCCTCGGCGGGGCCGCTGCCCATTCCCCTCGAGGTCATCAAA GGCGGAAGGCATCTGATTTTCTGTCACTCCAAGAAAAGTGTGACGAACTGGCTGCCAAACTGGTCGGCGGAGTGCTCGCCGGCTGCTGGCTATTG CCTCAGCACAGGCTGTGTGTCATCGTCGGCAGAATCGTCCTGTCCGGCAAACCCGCTTGCGAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCCTGA AGCCATGCCAGACCCAGATGGTTTTGGTTTTGCCTCCTGCTCAGCTCCAGCACAAGCGGAATCACAGGCGGATAACACAACCACAAGCTCCGAGCCTGC CCCTAGCGGATGCCCTCCCGATAGCGATGCCGAAAGGACACAGAGAAGGGGAAGGACAGGCAGAGGCAAACCCGGAATCTATAGGTTTGTGGCTCCCG CACCTCCAGGATAGGGATCAGGCTCAGGTCTGGGTCCCCCCCTCTGAATGTGAGAGGCCGAAGGGATGCCGTCATCCTCCTGATGTGCGTCGT GCATCCCACACTGGGAGTGAGAGCCACAAGGAAAACCTCCGAGAGAAGCCAACCCAGAGGCAGACGCAACCCATTCCCAAAGCCAGAAGGCCTGAGG CAAACGTCAGCGTCGCCCATGACGGAGCCGGAAAGAGAGTGTATTACCTCACCAGAGACCCTACCACACCCCTCGCCAGAGCCGCTTGGGAAAGCGAA CCCGCTCCCTCCGGCTGTCCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCCTCTGGAAGGCGAACCCGGAGACCCTATCGGAGGCCATTA CGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACCGGAACCTATGTGTATAACCATCTGACACCCCTCAGGGATCCCTCCACCGAAGACCTCGTGA ATCTGCTCCCCGCTATCCTCAGCCCTGGCGCTCTGGTCGTGGGAGTGGTCTGCGCTGCCATTCTGAGAATCCTCGACATGATCGCTGGCGCTCACTGG GGGAAGCAGACCCTCCTGGGGACCCACAGACCCTAGGAGAAGGTCCAGGAATTGGACAACCCCAAGGCTGTAACTGTAGCATTTACCCTGGCCATATCA 

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TCAGGGTCTGCGAAAAGATGATGGGATACATTCCCCTCGTGGGAGCCCCTCTGGGAGGCGCTGCCAGAGCCCTCGCCCATGGCGTCAGGGTCCTGGAA GACGGAGTGAATGGCGGAAACGCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCCGGAGCCAAACAGAATATCCAACTGATTAACACAAA GAGACAAAAACCAAGTGGAAGGCGAAGTGCAAATCGTCAGCACAGCCGCTCAGACATTCCTCGCCACATGCATTAACGGAGTGTGTCCCCGCTACCCAA CTGAGAAGGCATATCGATCTGCTCGTGGGAAGCGCTACCCTCTGCTCCGCCCTCTACGTCGGCGGATCTGTGTGGCTCCCACGCTCCCACAGGCTCCGG  ${\tt CAAAAGCACAAAGGTCCCCGCTGCCTATGCCGCTCAGGGATACAAAGTGCTCGTGCTCAACCCTAGCGTCAGGACATGGGCTCAGCCTGGCTATCCCT}$ GGCCCCTCTACGGAAACGAAGGCTGTGGCTGGGCCGGATGGCTCCTGTCCCCCAGAGGCCTCCACCGAAGACGTCGTGTGTTGCTCCATGTCCTACTCC TGGACAGGCGCTCTGGTCACCCCTTGCGCTGCCGAAGAGCCAAAAGCTCCCCATTGCCCTCGACACAGAGGTCGCCGCTAGCTGTGGCGGAGTGGTCCT TTGGCGGAGCCGGAAACAATACCCTCCACTGTCCCACAGCGTCGAGGGAAGCCTGTAGCCTCACCCCTCCCCATAGCGCTAAGTCCAAGTTTGGCTAT GGCTTTCACAGCCGCTGTGACACAGATTGTGGGAGGCGTCTACCTCCTGCCTAGGAGAGGCCCTAGGCTCGGCGTCAGGGCTACCAGAAAGACAAGCG AAAGGTCCCAGCCTCTGCATAGCTATAGCCCTGGCGAAATCAATAGGGTCGCCGCTTGCCTCAGGAAACTGGGAGTGCCTCCCCTCAGGGCTTGGAGA GAATCTGGAAACCACAATGAGAAGCCCTGTGTTTACCGATAACTCCAGCCCTCCCGCTGTGCCTCAGTCCTTCCAAGTGGCTCACCCCCACACCCCACACCCC CTGGCTCCGTGACAGTGCCTCACCCTAACATTGAGGAAGTGGCTCTGTCCACCGCGAAATCCCTTTCTATGGCAAACTGGTCTTCGATATCACA  ${\tt AAGCTCCTGCTCGCCCTCTGGACCCCTTGGATTCTGCAAGGCCTCCTGGTCAAGGTCCCCTATTTCGTCACCGCTGCCCTCGTGATTGGCCCAACTCCTCAAGGTCCCCTATTTCGTCACCGCTGCCCTGGTGATTGGCCCAACTCCTCAAGGTCCCCTATTTCGTCACCGCTGCCCTGGATTGGCCCAACTCCTCAAGGTCCCCTATTTCGTCACCGCTGCCCTGGATTGGCCCAACTCCTCAAGGTCCCCTATTTCGTCACCGCTGCCCTGGATTGGCCCCAACTCCTCAAGGTCCCCTATTTCGTCACCGCTGCCCTGGATTGGCCCCAACTCCTCAACTCCTCAACTCCAACTCCTCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCCAACTCAAC$ AACGAAGTGACACTGACACCCTGTGACAAAGTATATCATGACCTGTGCCAGGAGTGGCTATCAAAAGCCTCACCGAAAAGGCTCTACGTCGGCGGACC AACACCCTGAGGCTACCTATAGCAGATGCGGAACCTGTGGCTCCAGCGATCTGTATCTGGTCACCAGACACGCTGACGTCATCCCTGTGAGAAGGAGA GGCGATAGCAGAGGCTCCCTGCTCAACATGTGGTCCGGCACATTCCCTATCAATGCCTATACCACAGGCCCTTGCACACCCCTCCCGGCTCCCAATTA CACATTCGCTCTGTGGCACTCCACCGATGCCACAAGCATTCTGGCAATCGGAACCGTCCTGGATCAGGCTGAGACAGCCGGAGCCAGACTGGTCGTGC TOGCCACATACGTCCCCGAAAGCGATGCCGCTGCCAGAGTGACAGCCATTCTGTCCAGCCTCACCGTCACCCAACTGCTCAGGAGACTGCATCAGTGG AGGCCTAGCTGGGGCCCTACCGATCCCAGAAGGAGAAGCAGAAACCTCGGCAAAGTGATTGACACCTGACATGCGGATTCGCTGACCTCGGCCCTGA ATCTGCCTTACATTGAGCAAGGCATGATGCTCGCCGAACAGTTTAAGCAAAAGGCTCTGGGACTGCTCCAGACATACCAAGCCACAGTGTGTGCCAGA GCCCAAGCCCCTCCCCCTAGCTGGGACCAAATGTGGAAGTGTCTGATTAGGCTCAAGCCCTACCCTCTGCGGAATCGTCCCGCTAAGTCCGTGTGTGG GAGGATGTGGTCTGCTGTAGCATGAGCTATAGCTGGACCGGATGGGATCAGATGTGGAAATGCCTCATCAGACTGAAACCCACACTGCATGGCCCCTAC CCCTCTGCTCTACAGACTGGGAGCCGTCCAGAATCTGGCTGAGCAATTCAAACAGAAAGCCCTCGGCCTCCTGCAAACCGGCTAGCAGACAGGCTGAGG TCATCGCTCCCGCTGTGCAAACCAATTGGCAAAAGCTCGAGGTCTTCTGGGCCAAACACATGTGGAATTTCATTAGCGGAATCCAATACCTCGCCGGA CTGTCCACCCTCCCGGACTGATTGCCTTTGCCTCCAGGGGAAACCATGTGTCCCCCACACACTATGTGCCTGGGTCGGACGCCTGCCGCTAGGGTCAC CGCTATCCTCGCCACACTGTGTAGCGCTCTGTATGTGGGAGACCTCTGCGGAAGCGTCTTCCTCGTGGGACAGCTCTTCACATTCTCCCCCAGAAGGC ATAGCTCCGTGCTCTGCGAATGCTATGACGCTGGCTGGCCTGGTACGAACTGACACCCGCTGAGACAACCGTCAGGCTCAGGCCTTACATGGGCTGG GTGGCTGCCCAACTGGCTGCCCCTGGCGCTGCCACAGCCTTTGTGGGAGCCGGACTGGCTGCCGCTGCCATTGGCTCCGTGGGAAGCTGGCACATTAA CTCCACCGCTCTGAATTGCAATGAGTCCCTGAATACCGGATGGCTCGCCGGACTGTTTTACCAACACAAATTCAATAACGCTCTGTCCAACTCCCTGC TCAACAATACCAGACCCCCTCTGGGAAACTGGTTCGGATGCACAGTGCCTCCCCCTAGGAAAAAGAGAACCGTCGTGCTCACCGAAAGCACACTGTCC ACCECTCTGGCTGAGGTCGCCACAAGTCCTTCGGAAGCACACCTCCAGGTCGCCTGTCAGAGACAGAAAAAGGTCACCTTTGACAGACTGCAAGT GCTCGACTCCCACTATCAGGATGTGCTCGACCAAGCCGAAACCGCTGGCGCTAGGCTCGTGGTCTGCCTACCCCTACCCCTCCCGGAAGCGTCACCG TCCCCCATCCCAATATCGAATTCCATTACGTCACCGGAATGACAACCGATAACCTCAAGTGTCCCTGTCAGGTCCCCTCCCCCCAATTCTTTACCGAA CTCCCCTCCAGGCAAGCCGAAGTGATTGCCCCTGCCGTCCAGACAAACTGGCAGAAACTGGAAGTGTTTTTGGGCTAAGCATATGTGGAACTTTTGCA GAGCCTCCGGCGTCCTGACAACCTCCTGCGGAAACACACTGACATGCTATATCAAAGCCGGGGGCGCTTGCAGAGCCGCTGGCCTCTTCGATAGGCTC CAGGTCCTGGATAGCCATTACCAAGACGTCCTGAAAGAGGCTCAAGGCTGCCGCTAGCAAAGTGAAAGCCAATCTGCTCGGCCCTCTGACAAACTCCAG GGGAGAGATTGCGGATACAGAAGGTGTAGGGCTAGCGGAGTGCTCACCACAAGCTGTGGCAATACCCTCATCATGCACACAAGGTGTCACTGTGGCG CTGAGATTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGCAGAGAGGTCAGCTTTAGGGTCGGCCTCCACGAATACCCT GTGGGAAGCCAACTGCCTTGCGAACCCGAACCCGATGTGGCTGTGCTCACCTCCAAGGAAGTGAAAGCCGCTGCCTCCAAGGTCAAGGCTAACCTCCT GTCCGTGGAAGAGGCTTGCTCCCTGACACCCCCTCACTCCGCCAAAGGCAGAGACGCTGTGATTCTGCTCATGTGTGGTCCACCCTACCCTCGTGT AGCCCTCCCTCCATGGCTCCAGCCCTAGCCCTAGCCCTAGCCCTACCTCCTACCTCAAGGGAAGCTCCGGCGGACCCCTCCTGTGTCCCGCTGGCCATGC CGTCGGCATTTTCAGAGCCGCTGACTTTGACCAAGGCTGGGGCCCTATCTCCTACGCTAACGGAAGCCGGACCCGATCAGAGACCCTATTGCTGGCACT ATCCCCCTAGCCTAGGCATGTGGGACCCGGAGGGGGGCGCCCTCCAGTGGATGAATAGGCTCATCGCTTCGCTAGCAGAGGCAATCACGTCAGCCCCT ACCCATTGCCTCTGGATGATGCTCCTGATTAGCCAAGCCGAAGCCGCTCTGGAAAACCTCGTGATTCTGAATGCCGCTAGCCTCGCCGGAACCCCATAT CATTCCCGATAGGGAAGTGCTCTACAGAGAGTTTGACGAAATGGAAGAGTGTAGCCCAACACCTCCCCTATATCGAACAGGGAATGATGCTGATTCACC TCCACCAAAACATTGTGGATGTGCAATACCTCTACGGAGTGGGAAGCTCCATCGCTAGCTGGCCATTAAGTGGGAGTATGTGTCCCACGCTAGGCCT AGGIGGTTCTGGTTCTGCTCCTCCTCGCCGCTGGCGTCGGCATTTACCTCCTGCCTAACAGAGCCGCTGCCGCTACCCTCGGCTTTGGCGCTTA CATGAGCAAAGCCCATGGCATTGACCCTAACATTAGGACAGGCGTCAGGACAATCACAACCGGAAGGGTCCAGGGACTGCTCAGGATTTGCGCTCTGG CTAGGAAAATGATTGGCGGACACTATGTGCAAATGGCTATCATTAAGCTCGGCGCTAGGAGATTCGCTCAGGCTCTGCCTGTGTGGGCCAGACCCGAT TACANTCCCCCTCTGGTCGAGACATGGAAAAAGCCTGGCTATGAGCCTACCGCTGCCCAAACCTTTCTGGCTACCTGTATCAATGGCGTCTGCTGGAC CGTCTACCATGGCGCTGGCACAAGGACAATCGCTAGGCCTTAGGCCTCACAATGGCCTCAGGGATCTGGCTGTGGCTGTGGAACCCGTCGTGTTTAGCC AAATGGAAACCAAACTGATTACCTGGGGGGGCTTAAGGGACCCGTCATCCAAATGTATACCAATGTGGATCAGGATCTGGTCGGCTGGCCCGCTCCCCAA GATTCTGAGAAAGTCCCTGACAGGCACATACGTCTACAATCACCTCACCCCTCTGAGAGACTGGGCCCATAACGGACTGAGAGACCTCGCCGTCGCCG TCGAGCCTGTGTGTACCAGAGGCGTCGCCAAAGCCGTCGACTTTATCCCTGTGGAAAACCTCGAGACAACCATGAGGTCCCCCGTCTTCACAGACAAT GCCCTCGGCATTAACGCTGTGGCTTACTATAGGGGACTGGATGTGTCCGTGATTCCCACAAGCGGAGACGTCGTGGTCGTGGCTACCGATATGTCCGC

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ATACCGGAGACTTTGACTCCGTGATTGACTGTAACACATGCGTCACCCAAACCGTCGACTTTAGCCTCGACCCTAACACAAACAGAAGGCCTCAGGAT GTGAAATTCCCTGGCGGAGGCCAAATCGTCGGCGGAGTGTATCTGCTCCCCAGAAGGGGACCCAGAAGGGCTCTGGCTCACGGAGTGAGAGTGCTCGA GGATGGCGTCAACTATGCCACAGGCAATCTGCCTGGCTGTAGCTTTAGCATTTTCCTCAGCAAATTCGGATACGGAGCCAAAGACGTCAGGTGTCACG CTAGGAAAGCCGTCGCCCATATCAATAGCGTCTGGAAAGACCTCCTGGAAACCCCTGGCGCTAAGCAAAACATTCAGCTCATCAATACCAATGGCTCC TCATCTCCCAGGCTGAGGCTGCCCTCGACTGTGAGATTTACGGAGCCTGTTACTCCATCGAACCCCTCGACCTCCCCCCTATCATTCAGAGACTGCAT GGCCTCAGCGCTTTCTCCTGGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCCAAAGGCCCTGTGATTCAGATGTACACAAACGTCGA  ${\tt CCAAGACCTCTACAGATTCGTCGCCCCTGGCGAAAGGCCTAGCGGAATGTTTGACTCCAGCGTCCTGTGTGAGTGTTACGATGCCGGATGCGCTTGGT}$ ATAGGTCCGAGCTCAGCCCTCTGCTCCACCACACAGTGGCAGGTCCTGCCTTGCTCCTTCACAACCCTCCCCGGTCTGTCCACCGGACTGAGA AAGCTCGGCGTCCCCCCTCTGAGAGCCTGGAGGCATAGGGCTAGGTCCGTGAGAGGCCAGACTGCTCGCCAGAGGCGGAAGGGCTAGCCCTCTGACAAC CTCCCAGACACTGCTCTTCAATATCCTCGGCGGATGGGTCGCCGCTCAGCTCGCCGCTCCCGGAGCCGCTACCGCTCTGTGGATCCTCCAGGCTAGCC TCCTGAAAGTGCCTTACTTTGTGAGAGTGCAAGGCCTCCTGAGAATCTGTGCCCTCGCCAGAAAGATGGTGAAAAACGGAACCATGAGGATTGTGGGA  ${\tt CCCAGAACCTGTAGGAATATGTGGAGGGGAACCTTTCCCATTAACGCTTACACAACCGGAGAGGGTCGCCCTCAGCACACCGGAGAGATTCCCTTTTA$ CGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGCAGACACCTCATCTTTCTGACAAGGGATCCCACAACCCCTCTGGCTAGGGCTGCCTGGGAGA CAGCCAGACACCCCGTCAACTCCTGGCTCGGCAATATCATTAGGGTCAGCGCTGAGGAATACGTCGAGATTAGGAGAGTGGGAGACTTTCACTAT GTGACAGGCATGACCACAGACAATCTGAAATGCCCTCCCGTCGTGCATGGCTGTCCCCTCCCCGGAAGCCCCTCCCGTCCCCGTCCCAGAAA GAAAAGGACAGTGGTCCTGACAGAGTCCACCCTCAGCACAGCCCTCGCCGAACTGGCTACCAAAAGCTTTGGCTCCAGCTCCACCTCCGGCATTACCG GAGACAATACCACAACCTCCGTGTCCTGCCAAAGGGGATACAAAGGCGTCTGGAGAGGCGATGGCATTATGCATACCAGATGCCATTGCGGAGCCGAA ATCACAGGCCATGTGTTTCTGGTCGGCCAACTGTTTACCTTTAGCCCTAGGAGACACTGGACCACACAGGGATGCAATTGCTCCATCTATCCCGGACA CATTITCGTCGCCGCTGGCCTCGCCGGAGCCCCTATCGGAAGCGTCGGCCTCGGCAAAGTGCTCGTCGATATCCTCGCCGGATACCGGAGACACA TITGGGATTGGATTTGCGAAGTGCTCAGCGATTTCAAAACCTGGCTGAAAGCCCAAACTGATGCCCCAACTGCCAGCATTCCCTTTAACTCCAGCATT GTGTATGAGGCTGCCGATGCCATTCTGCATACCCCTGGCTGTGCCTTGCGTCAGGGAAGGCAATGCCTCCAGGTGTAGCTCCCGAAAG GCTCGCCTCCTGCAGAAGGCTCACCGATTTCGATCAGGGATGGGGACCCATTAGCTATGCCAATGGCTCCAGGACAGAGGGAAGCCATTTACCAATGCT  $\tt GTGACCTCGACCCTCAGGCTAGGGTCGCCATTAAGTCCCTGACAGAGAGACTGTTATGTGGGAGTGTCCCAAGGGATGGAGACTGCTCGCCCCTATCACA$ GCCTATGCCCAACAGAGAGAGGGACTGCTCGGCTGTATCATTACCTCCCTGACATTCTTTAGCGTCCTGATTGCCAGAGACCCAACTGGAACAGGCTCT GGATTGCGAAATCTATGGCGCTTGCTATAGCATTGAGCCTCTGGATTGCCAAGTGCCTAGCCCTGAGTTTTTCACAGAGCTCGACGGAGTGAGACTGC ATAGGTTTGCCCCTCCTGTAAGCCTCTGCTCAGGGAAACCTGTTACATTAAGGCTAGGGCTGCCTGTAGGGCTGCCGGACTGCAAGACTGTACCATG CTGGTCTGCGGAGACGATCTGGTCGTGATTATCGATCCCCAATATCAGAACCGGAGTGAGAACCATTACCACAGGCTCCCCCCATTACCTATAGCACATA CAGGCTCCCGGAGCCCTCGTGGTCGGCGTGTGTGCCGCTATCCTCAGGAGACACGTCGGCCCTGGCGAAGGCGCTGTGCAATGGATGAACAGACA CGATAGCCCTGACGCTGAGCTCATCGAAGCCAATCTGCTCTGGAGACAGGAAATGGGAGGCAATATCACAAGGGTCGAGTCCGAGAATGAGGGAGTGT TTACCGGACTGACACATTGACGCTCACTTTCTGTCCCAGACAAAGCAAAGCGGAGAGTTTCCCTTACCTCGTGGCTAGGGGAAGGAGACAGCCT ATCCCTAAGGCTAGGAGACCCGAAGGCAGAACCTGGGCCCAACCCGGATACCCTTGGCCTCTGTATGGCAATCTGATTGTGTTTCCCGATCTGGGAGT GAGAGTGTGTGAGAAAATGGCTCTGTATGACGTCGTGTCCAAGCTCCCCCTCGCCGTCATGGGATACGCTACCGGAAACCTCCCCGGATGCTCCTTCT GGCGTCGCCGGAGCCCTCGTGGCTTTCAAAATCATGAGCGGAGAGGTCAGCTATAGCTCCATGCCTCCCCTCGAGGGAGAGCCTGGCGATCCCGATCT GTCCGACGGAAGCTGGAGCACAGTGTCCAGCGAAGCCGGAAGGCAAGAGATGGGCGGAAACATTACCAGAGTGGAAAGCGAAAACAAAGTGGTCATCC TCGACTCCTTCGATCCCCTCGTGGCTGAGGAAGTGGGGATGGCCTGCCCCTCAGGGAAGCAGAAGCCTCACCCCTTGCACATGCGGAAGCTCCGACCTC TACCTCGTGACAAGGCATGCCGATGGCTGTAGCGGAGGCGCTTACGATATCATTATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCGG CATTGGCACAGTGCTCACCTTTACCATTGAGACAACCACACTGCCTCAGGATGCCGTCAGCAGAACCCCAAAGGAGAGGCAGAACCGGAAGGGGAAAGC CTGGCATTGACTGTTTCAGAAAGCATCCCGAAGCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTGGTCGACTATCCCTAT CTGGCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCCGCCTCTGTGACACCCCTGTGCCGCTGAGGAACAGAAACTGCCCTATCAATGCCCCT  ${\tt CAGCANTAGCCTCCTGAGACACCATAACCTCGTGTATATCTCCCAGCGAATGCACAACCCCTTGCTCCGGCTCCTGGCTCAGGGATATCTGGGACTGGA$ TCTGTGAGGTCCTGTCCGACTTTAAGACATGGCTCAAGGCTAAGCTCATGCCTCAGGCTCCCGGAATCCCTTTCGTCAGCCTGTCAGAGGGCTATAAG GGAGTGTGGGGGGGGGGGGGGGGGCGGACCCTGGATCACACCCAGATGCCTCGTGGATTACCCTTACAGACTGTGGCACTATCCCTGTACCATTAACTA TACCATTTTCAAA

HepC Savine Cassette Sequences (A+B+C) with specific restriction sites removed which can be joined to generate a single expressible open reading frame that encodes the hepc Savine protein above

#### Cassette A

## 145/216

CTGGGCTATCAAATGGGAATACGTCGTGCTCCTGTTTCTGCTCCTGGCTGACGCTAGGGTCTGCTCCCTGAATAACACAA GGCCTCCCCTCGGCAATTGGTTTGGCTGTACCTGGATGAATAGCACAGGCTTTACCAAAGTGTGTGGCGCTCCCCCTTTC ACAGAGGCTATGACAAGGTATAGCGCTCCCCCTGGCGATCCCCCTCAGCCTGAGTATGACCTCGAGCTCATCACAAGCTG TAGCTCCTGGCCTCCTGCTCCTGCTCCCCCCCAAAGGGCTTACGCTCTGGATACCGAAGTGGCTGCCTCCT GCGGAGGCGTCGTGCTCCAGCAAACCAGAGGCCTCCTGGGATGCATTATCACAAGCCTCACCGGAAGGGATAAGAATCAG GTCGAGGGAGAGGTCCAGATTGTGTCCAGCTCCCCCCTGCCGTCCCCCAAAGCTTTCAGGTCGCCCATCTGCATGCCCC TACCGGAAGCGGAAAGTCCACCAAAGTGCCTGCCGCTAACACACCCGGACTGCCTGTGTGTCAGGATCACCTCGAGTTTT GGGAAGGCGTCTTCACAGGCCTCACCCATATCGATGCCCCATTTCCTCGTGCTCCTGCTCTTCGCTGGCGTgGAtGCTGAG ACACACGTCACCGGAGGCAATGCCGGAAGGACAACCTCCGGCCTCGTGTCCCTGCTCGAGGTCACCCCTCACCCATCCCGT CACCAAATACATTATGACATGCATGAGGGCTGACCTCGAGGTCGTGACACAAGCACATGGGTCCTGGTCGTGGGACTGATGG CCCTCACCCTCAGCCCTTACTATAAGAGATACATTAGCTGGTGGCTGGTGGCTGCAATACTTTCTGACAAGGGTCGCC ATTTGCGGAAAGTATCTGTTTAACTGGGCCGTCAGGACAAAGCTCAAGCTCACCCCTATCGCTGCCGCTGGCAGACTGGA TCTGTCCATCGCTTACTTTAGCATGGTGGGAAACTGGGCCAAAGTGCTCGTGGTCCTGCTCCTGTTTGCCGGAGTGGATG ATGGGTCCCGGAGCCGTCTACGCTCTGTATGGCATGCAGCTCCCCTGTGAGCCTGAGCCTGACGTCGCCGTCCTGACAA GCATGCTGACAGACCCTAGCCATATCACAGCCGAAGCCGCTGGCAGAGACTCCGTGACACCCATTGACACAACCATTATG GCTAAGAATGAGGTCTTCTGTGCAACCCGAAAAGGGAGGCAGAAAGCCTGCCAGATACGCTGCCCAAGGCTATAAGGT CCGGACTGTATCACGTCACCAATGACTGTCCCAATAGCTCCATCGTCTACGAAGCCGCTGACGCTATCCTCCACACAGAGC TCCTACGGATTCCAATACTCCCCGGACAGAGAGTGGAGTTtCTCGTGCAAGCCCTGGAAGTCCAAGAAAACCCCTATGGG ATTCTCCGACACAGCCGCTTGCGGAGACATTATCAATGGCCTCCCCGTCAGCGCTAGGAGAGGCAGAGAGATTCTGCTCG GCCCTGCCGATGGCCATGAGCCAACTGTCCGCCCCTAGCCTCAAGGCTACCTGTACCGCTAACCATGACTCCCCGGATGCC GAACTGATTGAGGCTAACCTCCTGTGGAACCCTGCCATTGCCTCCCTGATGGCCTTTACCGCTGCCGTCACCTCCCCCCT CACCACAAGCCAAACCCTCCTGTTTAACATTCTGGGACTGGTCCAGGCTTGGAAAAGCCAAAAAGACACCCATGGGCTTTA CTCAGGAAAAGCAGAAGGTTTGCCCAAGCCCTCCCGTCTGGGCTAGGCCTGACTATATGTTTGCCCCTACCCTCTGGGC TAGGATGATCCTCATGACACACTTTTTCTCCGTGCTCATCGCTAGGGATCAGCTCGAGCAAGCCCTCAGCGTCATCCCTA CCTCCGGCGATGTGGTCGTCGCCACAGACGCTCTGATGACCGGATACACAGGCGATTTCGATAGCGTCATCGATTGC CATAGCAAAAAGAAATGCGATGAGCTCGCCGCTAAGCTCGTGGCTCTGGGAATCAATGCCGTCGCCTATTACAGAGGCCT ALGTCCAGTATCTGTATAAGGGAAGGTGGGTGCCTGGCGCTGTGTATGCCCTCTACGGAATGTGGCCCCTCCTGCTCCTG CTCCTGGCTCTGCCTCAGAGAGCCTATAGCCCTATCACATACTCCACCTATGGCAAATTCCTCGCCGATGGCGGATGCTC CGGCGGAGCCTATGACATTATCATTTGCGATGAGTGTGCCAGAAGCGTCAGGGCTAGGCTCCTGGCTAGGGGAGGCAGAG CCGCTATCTGTGGCAAATACCTCTTCAATTGGGCTGTGAGAACCAAAAAGGCTGTGGCTCACATTAACTCCGTGTGGAAG GATCTGCTCGAGGATAGCGTCACCCCTATCGATACCACAATCATGGCCCAAAAAACGAgTTLACACCCTCCCCGTCGTCGT CCTGTGTGAGAGAGGGAAACGCTAGCAGATGCTGGGTGGCTATGACACCCACAGTGGCTACCAGAGACGGAAAGCTCCAG GATTGCACAATGCTCGTGTGTGGCGATGACCTCGTCGTCATCTGTGAGTCCGCCGGAGTGCAAGAGGATGCCGCTAGCCT CAGGGCTGTGGCGCTCTGGTCGCCTTTAAGATTATGTCCGGCGAAGTGCCTAGCACAGAGGATCTGGTCAACCTCC TGCCTGCCATTCTGTCCTACGATACCAGATGCTTTGACTCCACCGTCACCGAAAGCGGTATCAGAACCGAAGAGGCTATC TATCAGTGTTGCGATCTcGAcCCCCAAGAGCTCACCCCTGCCGAAACCACAGTGAGACTGAGAGCCTATATGAATACCCC TGGCCTCCCGTCTGCCAAGACCATCTGGAgTTtTGGCCCCAACCCGAATACGATCTGGAACTGATTACCTCCTGCTCCA GCAATGTCCGTGGCTCACGATGGCGCTGGCAAAAGGGTCTACTATCTGGGAAAGGTCATCGATACCCTCACCTGTGGC TTTGCCGATCTGATGGGCTATATCCCTCTGGTCGGCGCCTCCCCTCGGCGAGCCGCTGCCATTCCCCTCGAGGTCATCAA AGGCGGAAGGCATCTGATTTTCTGTCACTCCAAGAAAAAGTGTGACGAACTGGCTGCCAAACTGGTCGGCGGAGTGCTCG CCGCTCTGCCTGTCCTCAGCACAGGCTGTGTGTCATCGTCGGCAGAATCGTCCTGTCCGGCAAACCCGCTTGC GAAAGCGCTGGCGTCCAGGAAGACGCTGCCTCCCTGAGAGCCTTTACCGAAGCCATGACCAGATACTCCGCCCCTCCCGG AGACCCTGGCTGGTTCACAGCCGGATACTCCGGCGGAGACATTTTACCATAGCGTCAGCCATGCCAGACCCAGATGGTTTT GGTTTTGCCTCCTGCTCAGCTCCAGCACAAGCGGAATCACAGGCGATAACACAACCACAAGCTCCGAGCCTGCCCCTAGC GGATGCCCTCCCGATAGCGATGCCGAAAGGACACAGAGAAGGGCAAGGACAGGCAGAGGCAAACCCGGAATCTTATAGGTT CCTGTAACTGEACCAGAGGCGAAAGGTGTGACCTCGAGGATAGGGATGAGGCTCAGCTCCACGTCTGGGTCCCCCCTCTG AATGTGAGAGGCGGAAGGGATGCCGTCATCCTCCTGATGTGCGTCGTGCATCCCACACTGGGAGTGAGAGCCACAAGGAA AACCTCCGAGAGAGCCAACCCAGAGGCAGAAGGCAACCCATTCCCAAAGCCAGAAGGCCTGAGGGAAACCTCAGCGTCG CCCATGACGGAGCCGGAAAGAGAGTGTATTACCTCACCAGAGACCCTACCACACCCCTCGCCAGAGCCGCTTGGGAAAGC GAACCCGCTCCCTCCGGCTGTCCCCCTGACTCCGACGCTGAGTCCTACTCCAGCATGCCCCCTCTGGAAGCCGGACCCGG AGACCCTATCGEAGGCCATTACGTCCAGATGGCCATTATCAAACTGGGAGCCCTCACCGGAACCTATGTGTATAACCATC TGACACCCCTCAGGGGACCCCTCCACCGAAGACCTCGTGAATCTGCTCCCCGCTATCCTCAGCCCCTGGCGCTCTGGTCGTG GGAGTGGTCTGCGCTGCCATTCTGAGAATCCTCGACATGATCGCTGGCGCTCACTGGGGGGGTCCTGGCTGCCATTGCCTA GCAGACCCTCCTGGGGACCCACAGACCCTAGGAGAAGGTCCAGGAATgtcgactgagaattcgcc

#### Cassette B

# 146/216

GCTGGCAGAACCACAAGCGGACTGGTCAGCCTCCTGACACCCGGAGCCAAACAGAATATCCAACTGATTAACACAAACGG ACTGGCTCTGCTCAGCTGTCTGACAGTGCCTGCCTCCGCCTATCAGGTCAGGAATAGCACAGGCCTCTACCATGTGACAA ACGATTGCCCTGGCAGAGACAAAAACCAAGTGGAAGGCGAAGTGCAAATCGTCAGCACAGCCGCTCAGACATTCCTCGCC ACATGCATTAACGGAGTGTGTCCCGCTACCCAACTGAGAAGGCCATATCGATCTGCTCGTGGGGAAGCGCTACCCTCTGCTC CGCCCTCTACGTCGGCGATCTGTGTGGCTCCCACGCTCCCACAGGCTCCGGCAAAAGCACAAAGGTCCCCGCTGCCTATG CCGCTCAGGGATACAAAGTGCTCGTGCTCAACCCTAGCGTCAGGACATGGGCTCAGCCTGGCCTCTGCCCCTCTAC GGAAACGAAGGCTGTGGCTGGGCCGGATGGCTCCTGTCCCCCAGAGGGCTCCACCGAAGACGTCGTGTTGCTTCCATGTC CTACTCCTGGACAGGCGCTCTGGTCACCCCTTGGGCTGCCGAAGAGCCAAAAGCTCCCCATTGCCCTCGACACAGAGGTCG CCGCTAGCTGTGGCGGAGTGGTCCTGGTCGGCCTCATGGCTCTGACACACTGTCCCCCTATTACAAAAGGTATTGGATGAAC TCCACCGGATTCACAAAGGTCTGCGGAGCCCCTCCCTGTGTGATTGGCGGGAGCCGGAAACAATACCCTCCACTGTCCCAC AAGCGTCGAGGAAGCCTGTAGCCTCACCCCTCCCCATAGCGCTAAGTCCAAGTTTGGCTATGGCGCTAAGGATGTGAGAT GCCATGCCAGAATCTCCGGCATTCAGTATCTGGCTGGCCTCAGCACACTGCCTGGCAATCCCGCTATCGCTAGCCTCATG GCTTTCACAGCCGCTGTGACACAGATTGTGGGAGGCGTCTACCTCCTGCCTAGGAGAGGCCCTAGGCTCCGCGTCAGGGC TACCAGAAAGACAAGCGAAAGGTCCCAGCCTCTGCATAGCTATAGCCCTGGCGAAATCAATAGGGTCGCCGCTTGCCTCA ATTATCATGTTCGCTCCCACACTGTGGGCCAGAATGATTCTGATGACCCATGAGAATCTGGAAACCACAATGAGAAGCCC TGTGTTTACCGATAACTCCAGCCCTCCGGCTGTGCCTCAGTCCTTCCAAGTGGCTCACCTCGCCACACCCCCTGGCTCCG TGACAGTGCCTCACCTAACATTGAGGAAGTGGCTCTGTCCACCACGGGGAAATCCCTTTCTATGGCAAACTGGTCTTC GATATCACAAAGCTCCTGCTCGCCGTCTTCGGACCCCTCTGGATTCTGCAAGCCTCCCTGCTCAAGCTCCCCTATTTTCTT CACCGCTGCCCTCGTGATGGCCCAACTGCTCAGGATTCCCCAAGCCATTCTGGATATGATTGCCGGAGCCCATTGGGGAG TGCTCGCCGGATGCAATACCTGTGTGACACAGACAGTGGATTTCTCCCTcGACCCCACATTCACAATCGAAACCACAACC CTCCCCAAGACGCTGTGTCCCACGGACCCACACCCCTCCTGTATAGGCTCGGCGCTGTGCAAAACGAAGTGACACTGAC ACACCCTGTGACAAAGTATATCATGACCTGTGCCAGAGTGGCTATCAAAAGCCTCACCGAAAGGCTCTACGTCGGCGGAC CCCTCACCAATAGCAGAGGCGAAAACTGTGGCTATAGGAGATGCGTCATCGGAGGCGCTGGCAATAACACACTGCATTGC CCTACCGATTGCTTTAGGAAACACCCTGAGGCTACCTATAGCAGATGCGGAACCTGTGGCTCCAGCGATCTGTATCTGGT CACCAGACACGCTGACGTCATCCCTGTGAGAAGGAGGCGGATAGCAGAGGCTCCCTGCTCAACATGTGGTCCGGCACAT TCCCTATCAATGCCTATACCACAGCCCTTGCACACCCTCCCCAATTACACATTCGCTCTGTGCCACTCCCAC GATGCCACAAGCATTCTGGGAATCGGAACCGTCCTGGATCAGGCTGAGACAGCCGGAGCCAGACTGGTCGTCGCCAC ATACGTCCCCGAAAGCGATGCCGCTGCCAGAGTGACAGCCATTCTGTCCAGCCTCACCGTCACCCAACTGCTCAGGAGAC TGCATCAGTGGAGGCCTAGCTGGGGCCCTACCGATCCCAGAAGGAGAAGCAGAAACCTCGGCAAAGTGATTGACACACTG ACATGCGGATTCGCTGACCTCGGCCCTGACCAAAGGCCTTACTGTTGGCATTACCCTCCCAAACCCTGTGGCATTGTGCC TGCCAAAAGCGTCTGCGGACCCGTCTACTGTGAGGAATGCTCCCAGCATCTGCCTTACATTGAGCAAGGCATGATGCTCC CCGAACAGTTTAAGCAAAAAGGCTCTGGGACTGCTCCAGACATTACCAAGCCACAGTGTGTGCCAGAGCCCCAAGCCCCTCCC CCTAGCTGGGACCAAATGTGGAAGTGTCTGATTAGGCTCAAGCCTACCCTCTGCGGAATCGTCCCCGCTAAGTCCGTGTG TGGCCCTGTGTATTGCTTTACCCCTAGCCCTGTGGTCGTGGGAACCACAGAAGCGGAAGCTCCCTGACAGTGACAC GATGGCTCCTGGTCCACCGTCAGCTCCGAGGCTGGCACAGAGGATGTGGTCTGCTGTAGCATGAGCTATAGCTGGACCGG ATGGGATCAGATGTGGAAATGCCTCATCAGACTGAAACCCACACTGCATGGCCCTACCCCTCTGCTCTACAGACTGGGAG CCGTCCAGAATCTGGCTGAGCAATTCAAACAGAAAGCCCTCCGGCCTCCTGCAAACCGCTAGCAGACAGGCTGAGGTCATC GCTCCCGCTGTGCAAACCAATTGGCAAAAGCTCGAGGTCTTCTGGGCCAAACACATGTGGAATTTCATTAGCGGAATCCA ATACCTCGCCGGACTGTCCACCCTCCCGGACTGATTGCCTTTGCCTCCAGGGGAAACCATGTGTCCCCCCACACACTATG TGCCTGAGTCCGACGCTGCCGCTAGGGTCACCGCTATCCTCGCCACACTGTGTAGCGCTCTGTATGTGGGAGACCTCTGC GGAAGCGTCTTCCTCGTGGGACAGCTCTTCACATTCTCCCCCAGAAGGCATAGCTCCGTGCTCTGCGAATGCTATGACGC TGGCTGTGCCTGGTACGAACTGACACCCGCTGAGACAACCGTCAGGCTCAGGGCTTACATGGGCTGGGTGGCTGCCCAAC ATTAACTCCACCGCTCTGAATTGCAATGAGTCCCTGAATACCGGATGGCTCGCCCGGACTGTTTTACCAACACACAAATTCAA TAACGCTCTGTCCAACTCCCTGCTCAGGCATCACAATCTGGTCTACTCCACCACAAGCAGAAGCGCTTGCCAAAGGCAAA AGAAAGTGACAGCCGCTATGTCCACCAATCCCAAACCCCAAAGGAAAACCCAAAAGGAATACCAATAGGAGACCCCAAGAC GTCAAGTTTCCCGGAGGCGGAAGCCAAACCAAACAGTCCGGCGAAAACTTTCCCTATCTGGTCGCCTATCAGGCTACCGT CTGCGCTAGGGCTCAGGCTCCCCCTCCCTCCCTACCTATAGCTGGGGCGCCTAACGATACCGATGTGTTTGTGCTCA ACAATACCAGACCCCCTCTGGGAAACTGGTTCGGATGCACAGTGCCTCCCCCTAGGAAAAAGAGAACCGTCGTGCTCACC GAAAGCACACTGTCCACCGCTCTGGCTGAGCTCGCCACAAAGTCCTTCGGAAGCACAACCTCCAGGTCCGCCTGTCAGAG ACAGAAAAAGGTCACCTTTGACAGACTGCAAGTGCTCGACTCCCACTATCAGGATGTGCTCGACCAAGCCGAAACCGCTG GCGCTAGGCTCGTGGCTACCGCTACCCCTCCCGGAAGCGTCACCGTCCCCATCCCAATATCGAgTTLCATTAC GTCACCGGAATGACAACCGGATAACCTCAAGTGTCCCCTGTCAGGTCCCCCCCGAGTTLTTTACCGAACTGGATGGCGT CCTGAAACTGACACCCATTGCCGGAAGGCTCGACCTCAGCGGATGGTTTACCGCTGGCTATAGCGGAGGCGATA TCTATCACTCCGCCTCCAGGCAAGCCGAAGTGATTGCCCCTGCCGTCCAGACAACTGGCAGAAACTGGAAGTGTTTTGG GCTAAGCATATGTGGAACTTTTGCAGAGCCTCCGGCGTCCTGACAACCTCCTGCGGAAACACACTGACATGCTATATCAA AGCCAGAGCCGCTTGCAGAGCCGCTGGCCTCTTCGATAGGCTCCAGGTCCTGGATAGCCATTACCAAGACGTCCTGAAAG AGGTCAAGGCTGCCGCTAGCAAAGTGAAAGCCAATCTGCTCGGCCCTCTGACAAACTCCAGGGGAGAGAATTGCGGATAC AGAAGGTGTAGGGGCTAGCGGAGTGCTCACCACAAGCTGTGGCAATACCCTCATCATGCACACAAGGTGTCACTGTGGGGG TGAGATTACCGGACACGTCAAGAATGGCACAATGAGAATCGTCGGCCCTAGGACATGCAGAGAGGGTCAGCTTTAGGGTCG GCCTCCACGAATACCCTGTGGGAAGCCAACTGCCTTGCGAACCCCGAACCCCGATGTGGCTGTGCTCACCTCCAAGGAAGTG AAAGCCGCTGCCTCCAAGGTCAAGGCTAACCTCCTGTCCGTGGAAGAGGCTTGCTCCCTGACACCCCCTCACTCCGCCAA AGGCAGAGACGCTGTGATTCTGCTCATGTGTGTGGTCCACCCTACCCTCGTGTTTGACATTACCAAACTGCTCCTGGCTG TGTTTGGCCCTATGCTCACGGATCCCTCCCACATTACCGCTCAGGCTGCCGGAAGGAGACTGGCTAGGGGAAGCCCTCCC TCCATGGCTAGCTCCAGCGCTAGCCCTAGGCCTATCTCCTACCTCAAGGGGAAGCTCCGGCGGACCCCTCCTGTGTCCCGC TGGCCATGCGGCATTTTCAGAGCCGCTGACTTTGACCAAGGCTGGGGCCCTATCTCCTACGCTAACGGAAGCGGAC COGATCAGAGACCCTATTGCTGGCACTATCCCCCTAAGCCTAGGCATGTGGGACCCGGAGAGGGAGCCGTCCAGTGGATG  ${\tt ANTAGGCTCATCGCTTAGCAGAGGCAATCACGTCAGCCCTACCCATCtcgagtgagaattcgcc}$ 

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Cassette C

ggcggatccaccatgctcgagTGCCTCTGGATGATGCTCCTGATTAGCCCAAGCCGGAGCCGCTCTGGAAAACCTCGTGAT TCTGAATGCCGCTAGCCTCGCCGGAACCCATATCATTCCCGATAGGGAAGTGCTCTACAGAGAGTTTGACGAAATGGAAG AGTGTAGCCAACACCTCCCCTATATCGAACAGGGAATGATGATGCTCATCACCTACCAAAAACATTGTGGATGTGCAATAC CTCTACGGAGTGGGAAGCTCCATCGCTAGCTGGGCCATTAAGTGGGAGTATGTGTCCCACGCTAGGCCTAGGTGGTTCTG GTTCTGTCTGCTCGCCGCCGCCGCGCGCATTTACCTCCTGCCTAACAGAGCCGCTGCCGCTACCTCGGCTTTG GCGCTTACATGAGCAAAGCCCATGGCATTGACCCTAACATTAGGACAGGCGTCAGGACAATCACAACCGGAAGGGTCCAG GGACTGCTCAGGATTTGCGCTCTGGCTAGGAAAATGATTGGCGGACACTATGTGCAAATGGCTATCATTAAGCTCGGCGC TAGGAGATTCGCTCAGGCTCTGCCTGTGTGGGCCAGACCCGATTACAATCCCCCTCTGGTCGAGACATGGAAAAAGCCTG ACTATGAGCCTACCGCTGCCCAAACCTTTCTGGCTACCTGTATCAATGGCGTCTGCTCGACCGTCTACCATGGCGCTCGC ACAAGGACAATCGCTAGCCCTTGGGCTCACAATGGCCTCAGGGATCTGGCTGTGGCTGTGGAACCCGTCGTGTTTAGCCA AATGGAAACCAAACTGATTACCTGGGGCGCTAAGGGACCCGTCATCCAAATGTATACCAATGTGGATCAGGATCTGGTCG GAAGAGGATGAGAGAGAGTTAGCGTCCCCGCTGAGATTCTGAGAAAGTCCCTGACAGGCACATACGTCTACAATCACCT CACCCCTCTGAGAGACTGGGCCCATAACGGACTGAGAGACCTCGCCGTCGCCGTCGAGCCTGTGTGTACCAGAGGCGTCG CCAAAGCCGTgGALTTTATCCCTGTGGAAAACCTCGAGACAACCATGAGGTCCCCGGTCTTCACAGACAATGCCCTCGGC ATTAACGCTGTGGCTTACTATAGGGGACTGGATGTCTCCGTGATTCCCACAAGCGGAGACGTCGTGGTCGTGGCTACCGA TATGTCCGCCGATCTGGAAGTGGTCACCTCCACCTGGGTGCTCGTGGGAGGCGTCCTGGCTGCCCGCCTCGCCGCTTACTGTC TGTCCACCGGAGCCCTCATGACAGGCTATACCGGAGACTTTGACTCCGTGATTGACTGTAACACATGCGTCACCCAAACC GTGGAETTTAGCCTCGACCCTAACACAAACAGAAGGCCTCAGGATGTGAAATTCCCTGGCGGAGGCCAAATCGTCGGCGG AGTGTATCTGCTCCCCAGAAGGGGACCCAGAAGGGCTCTGGCTCACGGAGTGAGAGTGCTCGAGGATGGCGTCAACTATG CCACAGGCAATCTGCCTGGCTGTAGCTTTAGCATTTTCCTCAGCAAATTCGGATACGGAGCCAAAGACGTCAGGTGTCAC GCTAGGAAAGCCGTCGCCCATATCAATAGCGTCTGGAAAGACCTCCTGGAAACCCCTGGCGCTAAGCAAAACATTCAGCT GCCTCTTCTATCAGCATAAGTTTAACTCCAGCGGATGCCCTGAGAGACACTGGCTAGCTGTAGGAGACTGACAGTGGTCCTG CGACTGTGAGATTTACGGAGCCTGTTACTCCATCGAACCCCTCGACCTCCCCCTATCATTCAGAGACTGCATGGCCTCA GCGCTTTCTCCTGGACAGTGTATCACGGAGCCGGAACCAGAACCATTGCCTCCCCCAAAGGCCCTGTGATTCAGATGTAC ACAAACGTGGAtCAAGACCTCTACAGATTCGTCGCCCCTGGCGAAAGGCCTAGCGGAATGTTTGACTCCAGCGTCCTGTG TGAGTGTTACGATGCCGGATGCGCTTGGTATAGGTCCGAGCTCAGCCCTCTGCTCCTGTCCACCACACAGTGGCAGGTCC TGCCTTGCTTCACAACCCTCCCGGTCTGTCCACCGGACTGAGAAAGCTCGGGGTCCCCCCTCTGAGAGCCTGGAGG CATAGGGCTAGGTCCGTGAGAGCCAGACTGCTCGCCAGAGGGCGGAAGGGCTAGCCCTCTGACAACCTCCCAGACACTGCT CTTCAATATCCTCGGCGGATGGGTCGCCGCTCAGCTCGCCGCTCCCGGAGCCGCTACCGCTCTGTGGATtCTCCAGGCTA GCCTCCTGAAAGTGCCTTACTTTGTGAGAGTGCAAGGCCTCCTGAGAAATCTGTGCCCTCGCCAGAAAGATGGTGAAAAAC GGAACCATGAGGATTGTGGGACCCAGAACCTGTAGGAATATGTGGAGCGGAACCTTTCCCATTAACGCTTACACAACCGG AGAGGTCGCCCTCAGCACAACCCGCAGAGATTCCCTTTTACGGAAAGGCTATCCCTCTGGAAGTGATTAAGGGAGGCAGAC ACCTCATCTTTCTGACAAGaGAcCCCCACAACCCCTCTGGCTAGGGCTGCCTGGGAGACAGCCAGACACCCCGTCAAC TCCTGGCTCGGCAATATCATTAGGGTCAGCGCTGAGGAATACGTCGAGATTAGGAGAGTGGGGAGACTTTCACTATGTGAC CCCCTCCCAGAAAGGACAGACGTCGTCCTGACAGGCTCCACCCTCACCACAGCCCTCGCCGAACTCGCCTACCAAAAGC TTTGGCTCCAGCTCCACCTCCGGCATTACCGGAGACAAAACCCACAACCTCCGTGTCCTGCCAAAGGGGATACAAAGGCGT CTGGAGAGGCGATGGCATTATGCAGATGCCAGTGCCGAGCCGAAATCACAGGCCATGTGTTTCTGGTCGGCCAAC TGTTTACCTTTAGCCCTAGGAGACACTGGACCACACAGGGATGCAATTGCTCCATCTATCCCGGACACATTTTCGTCGGC GCTGGCCTCGCCGGAGCCGCTATCGGAAGCGTCGGCCTCGGCAAAGTGCTCGTGGATATCCTCGCCGGATACGGAGCCGG AGACATTTGGGATTGGCGAAGTGCTCAGCGATTTCAAAACCTGGCTGAAAGCCAAACTGATGCCCCAACTGCCTG GCATTCCCTTTAACTCCAGCATTGTGTATGAGGCTGCCGATGCCATTCTGCATACCCCTGGCTGTGTGCCTTGCGTCAGG GAAGGCAATGCCTCCAGGTGTAGCTCCGGCTGTCCCGAAAGGCTCGCCTCCTGCAGAAGGCTCACCGATTTCGATCAGGG ATGGGGACCCATTAGCTATGCCAATGGCTCCAGGACAGAGGAAGCCATTTACCAATGCTGTGACCTCGACCCTCAGGCTA GGGTCGCCATTAAGTCCCTGACAGAGAGACTGTATGTGGGGAGTGTCCAAGGGATGGAGACTGCTCGCCCCCTATCACAGCC TATGCCCAACAGACAAGGGGACTGCTCGGCTGTATCATTACCTCCCTGACATTCTTTAGCGTCCTGATTGCCAGAGACCA **ACTGGAACAGGCTCTGGATTGCGAAATCTATGGCGCTTGCTATAGCATTGAGCCTCTGGATTGCCAAGTGCCTAGCCCTG** ATTAAGGCTAGGGCTGCCTGTAGGGCTGCCGGACTGCAAGACTGTACCATGCTGGTCTGCGGAGACGATCTGGTCGTCAT TATCGATCCCAATATCAGAACCGGAGTGAGAACCATTACCACAGGCTCCCCCATTACCTATAGCACATACGGAAAGTTTC TOGCTGACGGATGCAATTGGACAAGGGGGAGAGAGACGGATGCGATCTGGAAGACAGAGACAGAAGCGAACTGTCCCCCCTCCTG CTCAGCACAACCCAAACCGGACACAGAATGGCTTGGGATATGATGATGATGATTGGTCCCCCACAGCCGCTCTGGT CATGGCTCAGCTCCTGAGAATCCCTCAGGCCTCCCGGAGCCCTCGTGGTCGGCGTCGTGTGTCCCCCCTATCCTCAGGAGAC ACGTCGGCCTGGCGAAGGCGCTGTGCAATGGATGAACAGACACGATAGCCCTGACGCTGAGCTCATCGAAGCCAATCTG TGACGCTCACTTTCTGTCCCAGACAAAGCAAAAGCAGAGAATTTCCCTTACCTCGTGGCTAGCGGAAGGAGACAGCCTA TCCCTAAGGCTAGGAGCCCGAAGGCAGAACCTGGGCCCAACCCGGATACCCTTGGCCTCTGTATGGCAATCTGATTGTG TTTCCCGATCTGCGAGTGAGAGAGAGAGAAAATGGCTCTGTATGACGTCCCAAGCTCCCCCTCGCCGTCATGGG GCGCTTACCAACTGGGAAAGGTCCTGGT9GALATTCTGGCTGGCTATGGCGCTGGCCTCGCCGGAGCCCTCGTGGCTTTC AAGCTGGAGCACAGTGTCCAGCGAAGCCGGAAGGCAAGAGATGGGCGAAACATTACCAGAGTGGAAAGCGAAAACAAAG TGGTCATCCTCGACTCCTTCGATCCCCTCGTGGCTGAGGAAGTGGGATGGCCTGCCCCTCAGGGAAGCAGAAGCCTCACC CCTTGCACATGCGGAAGCTCCGACCTCTACCTCGTGACAAGGCATGCCGATGCCTGTAGCGGAGGCGCTTACGATATCAT TATCTGTGACGAATGCCATAGCACAGACGCTACCTCCATCCTCGGCACTGGCACAGTGCTCACCTTTACCATTGAGACAA CCACACTGCCTCAGGATGCCGTCAGCAGAACCCCAAAGGAGGCGGAAACCCGGAAGGCGGAAAGCCTGGCATTGACTGTTTC AGAAAGCATCCCGAAGCCACATACTCCAGGTGTGGCTCCGGCCCTTGGATTACCCCTAGGTGTCTGGTgGAtTATCCCTA TCTGGCTGCCGGAGTGGGAATCTATCTGCTCCCCAATAGGGCTGCCGCCCTCGTGACACCCTGTGCCGCTGAGGAACAGA

# 148/216

AACTGCCTATCAATGCCCTCAGCAATAGCCTCCTGAGACACCATAACCTCGTGTATATCTCCAGCGAATGCACAACCCCT TGCTCCGGCTCCTGGCTCAGGGATATCTGGGACTGGATCTGTGAGGTCCTGTCCGACTTTAAGACATGGCTCAAGGCTAA GCTCATGCCTCAGCTCCCCGGAATCCCTTTCGTCAGCTGTCAGAGAGGCTATAAGGGAGTGTGGAGGGGAGACGGAAGCG GACCCTGGATCACACCCAGATGCCTCGTGGATTACCCTTACAGACTGTGGCACTATCCCTGTACCATTAACTATACCATT TTCAAAagatctTGAgtcgacgaattcgcc

## 149/216

### Melanoma Savine design

Two savines - one containing scrambled melanocyte differentiation Ags
- one containing scrambled melanoma cancer specific Ags

Genes in melanocyte differentiation Savine

#### gp100

MDLVLKRCLLHLAVIGALLAVGATKVPRNQDWLGVSRQLRTKAWNRQLYPEWTEAQRLDCWRGGQVSLKVSNDGPTLI
GANASFSIALNFPGSQKVLPDGQVIWVNNTIINGSQVWGGQPVYPQETDDACIFPDGGPCPSGSWSQKRSFVYWKTW
GQYWQVLGGPVSGLSIGTGRAMLGTHTMEVTVYHRRGSRSYVPLAHSSSAFTITDQVPFSVSVSQLRALDGGNKHFLR
NQPLTFALQLHDPSGYLAEADLSYTWDFGDSSGTLISRALVVTHTYLEPGPVTAQVVLQAAIPLTSCGSSPVPGTTDG
HRPTAEAPNTTAGQVPTTEVVGTTPGQAPTAEPSGTTSVQVPTTEVISTAPVQMPTAESTGMTPEKVPVSEVMGTTLA
EMSTPEATGMTPAEVSIVVLSGTTAAQVTTTEWVETTARELPIPEPEGPDASSIMSTESITGSLGPLLDGTATLRLVK
RQVPLDCVLYRYGSFSVTLDIVQGIESAEILQAVPSGEGDAFELTVSCQGGLPKEACMEISSPGCQPPAQRLCQPVLP
SPACQLVLHQILKGGSGTYCLNVSLADTNSLAVVSTQLIMPGQEAGLGQVPLIVGILLVLMAVVLASLIYRRIMKQD
FSVPQLPHSSSHWLRLPRIFCSCPIGENSPLLSGQQV

#### MART

MPREDAHFIYGYPKKGHGHSYTTAEEAAGIGILTVILGVLLLIGCWYCRRRNGYRALMDKSLHVGTQCALTRRCPQEG FDHRDSKVSLQEKNCEPVVPNAPPAYEKLSAEQSPPPYSP

#### TRP-1

PAFLTWHRYHLLRLEKDMQEMLQEPSFSLPYWNFATGKNVCDICTDDLMGSRSNFDSTLISPNSVFSQWRVVCDSLED YDTLGTLCNSTEDGPIRRNPAGNVARPMVQRLPEPQDVAQCLEVGLFDTPPFYSNSTNSFRNTVEGYSDPTGKYDPAV RSLHNLAHLFLNGTGGQTHLSSQDPIFVLLHTFTDAVFDEWLRRYNADISTFPLENAPIGHNRQYNMVPFWPPVTNTE MFVTAPDNLGYTYE

#### Tyros

MLLAVLYCLLWSFQTSAGHPPRACVSSKNLMEKECCPPWSGDRSPCGQLSGRGSCQNILLSNAPLGPQFPFTGVDDRE SWPSVFYNRTCQCSGNFMGFNCGNCKFGFWGPNCTERRLLVRRNIFDLSAPEKDKFFAYLTLAKHTISSDYVIPIGTY GQMKNGSTPMFNDINIYDLFVWMHYYVSMDALLGGSBIWRDIDFAHEAPAFLPWHRLFILRWEQEIQKLTGDENFTIP YWDWRDAEKCDICTDEYMGGQHPTNPNLLSPASFFSSWQIVCSRLEEYNSHQSLCNGTPEGPLRRNPGNHDKSRTPRL PSSADVEFCLSLTQYESGSMDKAANFSFRNTLEGPASPLTGIADASQSSMHNALHIYMNGTMSQVQGSANDPIFLLHH AFVDSIFEQWLQRHRPLQEVYPEANAPIGHNRESYMVPFIPLYRNGDFFISSKDLGYDYSYLQDSDPDSFQDYIKSYL EQASRIWSWLLGAAMVGAVLTALLAGLVSLLCRHKRKQLPEEKQPLLMEKEDYHSLYQSHL

### TRP2

MSPLWWGFLLSCLGCKILPGAQGQFPRVCMTVDSLVNKECCPRLGAESANVCGSQQGRGQCTEVRADTRPWSGPYILR NQDDRELWPRKFFHRTCKCTGNFAGYNCGDCKPGWTGPNCERKKPPVIRQNIHSLSPQEREQFLGALDLAKKRVHPDY VITTQHWLGLLGPNGTQPQFANCSVYDFFVWLHYYSVRDTLLGPGRPYRAIDFSHQGPAFVTWHRYHLLCLERDLQRL IGNESFALPYWNFATGRNECDVCTDQLFGAARPDDPTLISRNSRFSSWETVCDSLDDYNHLVTLCNGTYEGLLRRNQM GRNSMKLPTLKDIRDCLSLQKFDNPPFFQNSTFSPRNALEGFDKADGTLDSQVMSLHNLVHSFLNGTNALPHSAANDP IFVVLHSFTDAIFDEWMKRPNPPADAWPQELAPIGHNRMYNMVPFFPPVTNEELFLTSDQLGYSYAIDLPVSVEETPG WPTTLLVVMGTLVALVGLFVLLAFLQYRRLRKGYTPLMETHLSSKRYTEEA

#### MC1R

MAVQGSQRRLLGSLNSTPTAIPQLGLAANQTGARCLEVSISDGLFLSLGLVSLVENALVVATIAKNRNLHSPMYCPIC CLALSDLLVSGTNVLETAVILLLEAGALVARAAVLQQLDNVIDVITCSSMLSSLCFLGAIAVDRYISIFYALRYHSIV TLPRAPRAVAAIWVASVVFSTLPIAYYDHVAVLLCLVVFFLAMLVLMAVLYVHMLARACQHAQGIARLHKRQRPVHQG FGLKGAVTLTILLGIFFLCWGPPFLHLTLIVLCPEHPTCGCIFKNFNLFLALIICNAIIDPLIYAFHSQELRRTLKEV LTCSW

#### MUC1 P

MTPGTQSPFFLLLLLTVLTVVTGSGHASSTPGGEKETSATQRSSVPSSTEKNAVSMTSSVLSSHSPGSGSSTTQGQDV TLAPATEPASGSAATWGQDVTSVPVTRPALGSTTPPAHDVTSAPDNK

Figure 27

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#### MUC1R

NRPALGSTAPPVHNVTSASGSASGSASTLVHNGTSARATTTPASKSTPFSIPSHHSDTPTTLASHSTKTDASSTHHSS
VPPLTSSNHSTSPQLSTGVSFFFLSFHISNLQFNSSLEDPSTDYYQELQRDISEMFLQIYKQGGFLGLSNIKFRPGSV
VVQLTLAFREGTINVHDVETQFNQYKTEAASRYNLTISDVSVSDVPFPFSAQSGAGVPGWGIALLVLVCVLVALAIVY
LIALAVCQCRRKNYGQLDIFPARDTYHPMSEYPTYHTHGRYVPPSSTDRSPYEKVSAGNGGSSLSYTNPAVAAASANL

NB Muc 1 Repeat sequences in the middle of the gene were removed

Genes in melanoma specific Savine

BAGE

MAARAVFLALSAQLLQARLMKEESPVVSWRLEPEDGTALCFIF

GAGE-1

MSWRGRSTYRPRPRRYVEPPEMIGPMRPEQFSDEVEPATPEEGEPATQRQDPAAAQEGEDEGASAGQGPKPEADSQEQ GHPQTGCECEDGPDGQEMDPPNPEEVKTPEEEMRSHYVAQTGILWLLMNNCFLNLSPRKP

gp100In4

 ${\tt SWSQKRSFVYVWKTWGEGLPSQPIIHTCVYFFLPDHLSFGRPFHLNFCDFL}$ 

#### MAGE-1

MSLEQRSLHCKPEEALEAQQEALGLVCVQAATSSSSPLVLGTLEEVPTAGSTDPPQSPQGASAFPTTINFTRQRQPSE GSSSREEEGPSTSCILESLFRAVITKKVADLVGFLLLKYRAREPVTKAEMLESVIKNYKHCFPEIFGKASESLQLVFG IDVKBADPTGHSYVLVTCLGLSYDGLLGDNQIMPKTGFLIIVLVMIAMEGGHAPEEEIWEELSVMEVYDGREHSAYGE PRKLLTQDLVQEKYLEYRQVPDSDPARYEFLWGPRALAETSYVKVLEYVIKVSARVRFFFPSLREAALREEEEGV

#### MAGE-3

MPLEQRSQHCKPEEGLEARGEALGLVGAQAPATEEQEAASSSSTLVEVTLGEVPAAESPDPPQSPQGASSLPTTMNYP LWSQSYEDSSNQEEEGPSTPPDLESEFQAALSRKVAELVHFLLLKYRAREPVTKAEMLGSVVGNWQYFFPVIFSKASS SLQLVFGIELMEVDPIGHLYIFATCLGLSYDGLLGDNQIMPKAGLLIIVLAIIAREGDCAPEEKIWEELSVLEVFEGR EDSILGDPKKLLTQHFVQENYLEYRQVPGSDPACYEFLWGPRALVETSYVKVLHHMVKISGGPHISYPPLHEWVLREG EE

#### PRAME

MERRRLWGSIQSRYISMSVWTSPRRLVELAGQSLLKDEALAIAALELLPRELFPPLFMAAFDGRHSQTLKAMVQAWPF
TCLPLGVLMKGQHLHLETFKAVLDGLDVLLAQEVRPRRWKLQVLDLRKNSHQDFWTVWSGNRASLYSFPEPEAAQPMT
KKRKVDGLSTEAEQPFIPVEVLVDLFLKEGACDELFSYLIEKVKRKKNVLRLCCKKLKIFAMPMQDIKMILKMVQLDS
IEDLEVTCTWKLPTLAKFSPYLGQMINLRRLLLSHIHASSYISPEKBEQYIAQFTSQFLSLQCLQALYVDSLFFLRGR
LDQLLRHVMNPLETLSITNCRLSEGDVMHLSQSPSVSQLSVLSLSGVMLTDVSPEPLQALLERASATLQDLVFDECGI
TDDQLLALLPSLSHCSQLTTLSFYGNSISISALQSLLQHLIGLSNLTHVLYPVPLESYEDIHGTLHLERLAYLHARLR
ELLCELGRPSMVWLSANPCPHCGDRTFYDPEPILCPCFMPN

#### TRP2 IN2

LMETHLSSKRYTEEAGGFFPWLKVYYYRFVIGLRVWQWEVISCKLIKRATTRQP

#### NYNSO1a

MQAEGRGTGGSTGDADGPGGPGIPDGPGGNAGGPGEAGATGGRGPRGAGAARASGPGGGAPRGPHGGAASGLNGCCRC GARGPESRLLEFYLAMPFATPMEABLARRSLAQDAPPLPVPGVLLKEFTVSGNILTIRLTAADHRQLQLSISSCLQQL SLLMWITQCFLPVFLAQPPSGQRR

## NYNSO1b

MLMAQEALAPLMAQGAMLAAQERRVPRAAEVPGAQGQQGPRGREEAPRGVRMAARLQG

LAGE1

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MQAEGQGTGGSTGDADGPGGPGIPDGPGGNAGGPGEAGATGGRGPRGAGAARASGPRGGAPRGPHGGAASAQDGRCPC GARRPDSRLLQLHITMPFSSPMEAELVRRILSRDAAPLPRPGAVLKDFTVSGNLLFIRLTAADHRQLQLSISSCLQQL SLLMWITQCFLPVPLAQAPSGQRR

```
Differentiation Savine Scramble process
Disease name
               : melanoma
Input filename
             : Diffmucg.txt
Output filename : Diffmucs.txt
Number genes
Number segments : 187
Segment length
              : 30
Segment overlap : 15
Segments in original order:
Gene
        : gp100
Segment#
        : 1
1st Codon : 1
 A A M D L V L K R C L L H L A V I G A L L A V G A T K V P R
GCCGCTATGGATCTGGTCCTGAAAAGGTGTCTCCACCTCGCCGTCATCGGAGCCCTCCTGGCTGTGGGAGCCACAAAGGTCCCCAGA
Gene
         : gp100
Segment# : 2
Offset
        : 16
1st Codon : 1
 V I G A L L A V G A T K V P R N Q D N L G V S R Q L R T K A
GTGATTGGCGCTCTGCCCGCGCCTACCAAAGTGCCTAGGAATCAGGATTGGCTCGGCGTCAGCAGACAGCTCAGGACAAAGGCT
Gene
        : gp100
Segment# : 3
Offset
        : 31
N Q D W L G V S R Q L R T K A W N R Q L Y P E W T E A Q R L
AACCAAGACTGGCTGGGAGTGTCCAGGCÄACTGAGAACCAAAGCCTGGAACAGACAGCTCTACCCTGAGTGGACCGAAGCCCAAAGGCTC
Gene
        : gp100
Segment# : 4
Offset
        : 46
1st Codon : 1
W N R Q L Y P B W T E A Q R L D C W R G G Q V S L K V S N D
: gp100
Gene
Segment# : 5
Offset
        : 61
D C W R G G Q V S L R V S N D G P T L I G A N A S F S I A L
GACTGTTGGAGAGGCGGACAGGTCAGCCTCAAGGTCAGCAATGACGGACCCCACACTGATTGGCGCTAACGCTAGCCTTTAGCATTGCCCTC
Gene
        : gp100
Segment# : 6
Offset
        : 76
1st Codon : 1
G P T L I G A N A S P S I A L N P P G S Q K V L P D G Q V 1
GGCCCTACCCTCATCGGAGCCAATGCCTCCTTCTCCATCGCTCTGAATTTCCCTGGCTCCCAGAAAGTGCTCCCCGATGGCCAAGTGATT
Gene
        : gp100
Segment# : 7
Offset
        : 91
N F P G S Q K V L P D G Q V I W V N N T I I N G S Q V W G G
AACTTTCCCGGAAGCCAAAAGGTCCTGCCTGACGGACAGGTCATCTGGGTGAATAACACAATCATTAACGGAAGCCAAGTGTGGGGCGGA
Gene
        : gp100
Segment# : 8
Offset
       : 106
1st Codon : 1
```

Figure 27 (Cont)

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W V N N T I I N G S Q V W G G Q P V Y P Q E T D D A C I F P  ${\tt TGGGTCAACAATACCATTATCAATGGCTCCCAGGTCTGGGGAGGCCCAACCCGTCTACCCTCAGGAAACCGATGACGCTTGCATTTTCCCT\\$ Gene : qp100 Segment# : 9 Offset : 121 1st Codon : 1 Q P V Y P Q E T D D A C I F P D G G P C P S G S W S Q K R S CAGCCTGTGTATCCCCAAGAGACAGACGATGCCTGTATCTTTCCCGATGGCGGACCCTGTCCCTCCGGCTCCTGGTCCCAGAAAAGGTCC Gene : gp100 Segment# : 10 Offset : 136 1st Codon : 1 D G G P C P S G S W S Q K R S P V Y V W K T W G Q Y W Q V L GACGGAGGCCCTTGCCCTAGCGGAAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGGGAAGACATGGGGACAGTATTGGCAAGTGCTC Gene : gp100 Segment# : 11 Offset : 151 1st Codon : 1 PVYVWKTWGQYWQVLGGPVSGLSIGTGRAM TTCGTCTACGTCTGGAAAACCTGGGGCCAATACTGGCAGGTCCTGGGAGGCCCTGTGTCCGGCCTCAGCATTGGCACAGGCAGAGCCATG Gene : qp100 Segment# : 12 : 166 1st Codon : 1 G G P V S G L S I G T G R A M L G T H T M E V T V Y H R R G GECGGACCCGTCAGCGGACTGTCCATCGGAACCGGAAGGGCTATGCTCGGCACACCACAATGGAAGTGACAGTGTATCACAGAAGGGGA Gene : gp100 Segment# : 13 Offset : 181 1st Codon : 1 LGTHTMEVTVYHRRGSRSYVPLAHSSSAFT CTGGGAACCCATACCATGGGGTCACCGTCTACCATAGGAGGGCTCCAGGGTCCTACGTCCCCCTCGCCCCATAGCTCCAGGGGTTTCACA Gene : gp100 Segment# : 14 Offset : 196 1st Codon : 1 S R S Y V P L A H S S S A P T I T D Q V P F S V S V S Q L R AGCAGAAGCTATGTGCCTCTGGCTCACTCCAGCTCCGCCTTTACCATTACCGATCAGGTCCCCTTTAGCGTCAGCGTCAGCCAACTGAGA Gene : gp100 Segment# : 15 Offset : 211 1st Codon : 1 I T D Q V P P S V S V S Q L R A L D G G M K H P L R M Q P L Gene : gp100 Segment# : 16 Offset : 226 A L D G G N K H P L R N Q P L T F A L Q L H D P S G Y L A E GCCCTCGACGGAGGCAATAAGCATTTCCTCAGGAATCAGCCTCTGACATTCGCTCTGCAACTGCATGACCCTAGCGGATACCTCGCCGAA Gene : gp100 Segment# : 17 Offset : 241 1st Codon : 1 T P A L Q L H D P S G Y L A E A D L S Y T N D P G D S S G T ACCTTTGCCCTCCAGGTCCCTCCGGGCTATCTGGCTGAGGCTGACCTTCAGCTATACCTGGGACTTTGGCGATAGCTCCGGCACA Gene : gp100 Segment# : 18 Offset : 256 1st Codon : 1 A D L S Y T W D F G D S S G T L I S R A L V V T H T Y L E P 

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Gene : gp100 Segment# : 19 : 271 1st Codon : 1 LISRALVVTHTYLBPGPVTAQVVLQAAIPL  $\tt CTGATTAGCAGAGCCCTCGTGGTCACCCATACCTATCTGGAACCCGGACCCGTCACCGCTCAGGTCGTGCTCCCAGGCTGCCATTCCCCTC$ : gp100 Segment# : 20 Offset : 286 1st Codon : 1 G P V T A Q V V L Q A A I P L T S C G S S P V P G T T D G H GGCCCTGTGACAGCCCAAGTGGTCCTGCAAGCCGCTATCCCTCTGACAAGCTGTGGCTCCAGCCCTGTGCCTGGCACAACCGATGGCCAT Gene : qp100 Segment# : 21 Offset : 301 1st Codon : 1 T S C G S S P V P G T T D G H R P T A B A P N T T A G Q V P ACCTCCTGCGGAAGCTCCCCGGTCCCCGGAACCACAGACGGACACAGACCCACAGCCCGAAGCCCCTAACACCACCGCTGGCCAAGTGCCT Gene : gp100 Segment# : 22 Offset : 316 1st Codon : 1 R P T A E A P N T T A G Q V P T T E V V G T T P G Q A P T A AGGCCTACCGCTGAGGCTCCCAATACCACAGCCGGACAGGTCCCCACAACCGAAGTGGTCGGCACAACCCCTGGCCAAGCCCCTACCGGT : qp100 Segment# : 23 Offset : 331 1st Codon : 1 T T E V V G T T P G Q A P T A E P S G T T S V Q V P T T E V ACCACAGAGGTCGTGGGAACCACACCCGGACAGGCTCCCACAGCCGAACCCTCCGGCACAACCTCCGTGCAAGTGCCTACCACAGAGGTC : qp100 Segment# : 24 Offset : 346 1st Codon : 1 E P S G T T S V Q V P T T E V I S T A P V Q M P T A E S T G GAGCCTAGCGGAACCACAAGCGTCCAGGTCCCCACAACCGAAGTGATTAGCACAGCCCCTGTGCAAATGCCTACCGCTGAGTCCACCGGA Gene : gp100 Segment# : 25 Offset : 361 1st Codon : 1 I S T A P V Q M P T A B S T G M T P B K V P V S B V M G T T ATCTCCACCGCTCCCGTCCAGATGCCCACAGCCGAAAGCACAGGCATGACCCCTGAGAAAGTGCCTGTGTCCGAGGTCATGGGAACCCACA Gene : gp100 Segment# : 26 Offset : 376 1st Codon : 1 M T P B K V P V S B V M G T T L A B M S T P B A T G M T P A ATGACACCCGAAAAGGTCCCCGTCAGCGAAGTGATGGCCACAACCCTCGCCGAAATGTCCACCCCTGAGGCTACCGGAATGACACCCCGCT : gp100 Segment# : 27 Offset : 391 1st Codon : 1 LABMSTPEATGMTPAEVSIVVLSGTTAAQV CTGGCTGAGATGAGCACACCCGAAGCCACAGGCATGACCCCTGCCGAAGTGTCCATCGTCGTGCTCAGCGGAACCACAGCCGCTCAGGTC Gene : gp100 Segment# : 28 : 406 Offset 1st Codon : 1 B V S I V V L S G T T A A Q V T T T B W V B T T A R E L P I 

Figure 27 (Cont)

Gene

: qp100

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Segment# : 29 : 421 1st Codon : 1 TTTBNVETTARELPIPEPEGPDASSINSTE ACCACAACCGAATGGGTCGAGACAACCGCTAGGGAACTGCCTATCCCTGAGGGAGCCCGATGCCTCCAGCATTATGTCCACCGAA : gp100 Segment# : 30 Offset : 436 1st Codon : 1 PEPEGPDASSIMSTESITGSLGPLLDGTAT Gene : gp100 Segment# : 31 Offset : 451 1st Codon : 1 S I T G S L G P L L D G T A T L R L V K R Q V P L D C V L Y AGCATTACCGGAAGCCTCGGCCCTCTGCTCGACGGAACCGCTACCCTCAGGCTCGTGAAAAGGCAAGTGCCTCTGGATTGCGTCCTGTAT Gene : gp100 Segment# : 32 Offset : 466 1st Codon : 1 LRLVKRQVPLDCVLYRYGSFSVTLDIVQGI CTGAGACTGGTCAAGAGACAGGTCCCCCTCGACTGTGTGCTCTACAGATACGGAAGCTTTAGCGTCACCCTCGACATTGTGCAAGGCATT Gene : gp100 Segment# : 33 Offset : 481 1st Codon : 1 RYGSFSVTLDIVQGIESAEILQAVPSGEGD AGGTATGGCTCCTTCTCCGTGACACTGGATATCGTCCAGGGGAATCGAAAGCGCTGAGATTCTGCAAGCCGTCCCCTCCGGCGAAGGCGAT Gene : qp100 Segment# : 34 Offset : 496 1st Codon : 1 B S A E I L Q A V P S G E G D A F E L T V S C Q G G L P K E GAGTCCGCCGAAATCCTCCAGGCTGTGCCTAGCGGAGAGGGGAGACGCTTTCGAACTGACAGTGTCCTGCCAAGGCGGACTGCCTAAGGAA Gene : qp100 Segment# : 35 Offset : 511 1st Codon : 1 A P B L T V S C Q G G L P K B A C N B I S S P G C Q P P A Q GCCTTTGAGCTCACCGTCAGCTGTCAGGGAGGCCTCCCCAAAGAGGCTTGCATGGAGATTAGCTCCCCGGATGCCAACCCCCTGCCCAA Gene : gp100 Segment# : 36 Offset : 526 1st Codon : 1 A C M E I S S P G C Q P P A Q R L C Q P V L P S P A C Q L V Gene : qp100 Segment# : 37 Offset : 541 1st Codon : 1 R L C Q P V L P S P A C Q L V L H Q I L K G G S G T Y C L N AGGCTCTGCCAACCCGTCCTGCCTAGCCCTGCCTGTCAGCTCGTGCTCCACCAAATCCTCAAGGGAGGCTCCGGCACATACTGTCTGAAT : gp100 Gene Segment# : 38 : 556 Offset 1st Codon : 1 L H Q I L K G G S G T Y C L N V S L A D T N S L A V V S T Q CTGCATCAGATTCTGAAAGGCCGGAACCGGAACCTATTGCCTCAACGTCAGCCTCGCCGATACCAATAGCCTCGCCGTCGTGTCCACCCAA Gene : gp100 Segment# : 39

Figure 27 (Cont)

Offset

: 571

# 155/216

```
1st Codon : 1
 V S L A D T N S L A V V S T Q L I M P G Q E A G L G O V P L
 GTGTCCCTGGCTGACACAAACTCCCTGGCTGTGGTCAGCACACACGCTCATCATGCCCGGACAGGAAGCCGGACTGGGACAGGTCCCCCTC
Gene
         : gp100
Segment# : 40
 Offset
        : 586
1st Codon : 1
 LIMPGQBAGLGQVPLIVGILLVLMAVVLAS
CTGATTATGCCTGGCCAAGAGGCTGGCCTCGGCCAAGTGCCTCTGATTGTGGGAATCCTCCTGGTCCTGATGGCCGTCGTCCTCCC
Segment# : 41
        : 601
Offset
1st Codon : 1
 I V G I L L V L M A V V L A S L I Y R R R L M K Q D F S V P
ATCGTCGCCATTCTGCTCGTCGCTCATGGTCCTGGCTCATCTATAGGAGAAGGCTCATGAAACAGGATTTCTCCGTGCCT
        : gp100
Segment# : 42
Offset
        : 616
1st Codon : 1
 LIYRRRLMKQDFSVPQLPHSSSHWLRLPRI
CTGATTTACAGAAGGAGCTGATGAAGCAAGACTTTAGCGTCCCCCAACTGCCTCACTCCAGCTCCCACTGGCTGAGACTGCCTAGGATT
        : gp100
Segment# : 43
Offset
        : 631
1st Codon : 1
 Q L P H S S S H W L R L P R I F C S C P I G B N S P L L S G
CAGCTCCCCCATAGCTCCAGCCATTGGCTCAGGCTCCCCAGAATCTTTTGCTCCTGCCCTATCGGAGAGAATAGCCCTCTGCTCAGCGGA
        : gp100
Segment# : 44
Offset
        : 646
1st Codon: 1
FCSCPIGENSPLLSGQQVAA
TTCTGTAGCTGTCCCATTGGCGAAAACTCCCCCCTCCTGTCCGGCCAACAGGTCGCCGCT
        : MART
Gene
Segment# : 1
Offset
1st Codon : 1
AAMPREDAHFIYGYPKKGHGHSYTTAEEAA
GCCGCTATGCCTAGGGAAGACGCTCACTTTATCTATGGCTATCCCAAAAAGGGACACGGGACACTCCTACACAACCGCTGAGGAAGCCGCT
Gene
        : MART
Segment# : 2
Offset
       : 16
1st Codon : 1
K K G H G H S Y T T A E E A A G I G I L T V I L G V L L I
AAGAAAGGCCATGCCCATAGCCATACCACAGCCGAAGAGGCCTGCCGGAATCGGAATCCTCACCGTCATCCTCGGCGTCCTGCTCCTGATT
        : MART
Gene
Segment# : 3
Offset
       : 31
1st Codon : 1
G I G I L T V I L G V L L I G C W Y C R R N G Y R A L M
GGCATTGGCATTCTGACAGTGATTCTGGGAGTGCTCCTGCTCATCGGATGCTGGTACTGTAGGAGAAGGAATGGCTATAGGGCTCTGATG
       : MART
Gene
Segment# : 4
Offset
       : 46
1st Codon : 1
G C W Y C R R R R G Y R A L M D K S L H V G T Q C A L T R R
GGCTGTTGGTATTGCAGAAGGAGAAACGGATACAGAGCCCTCATGGATAAGTCCCTGCATGTGGGAACCCAATGCGCTCTGACAAGGAGA
Gene
        : MART
Segment# : 5
Offset
       : 61
1st Codon : 1
D K S L H V G T Q C A L T R R C P Q E G F D H R D S K V S L
```

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```
Gene
        : MART
Segment# : 6
Offset
        : 76
1st Codon : 1
 C P Q B G F D H R D S K V S L Q E K N C E P V V P N A P P A
TGCCCTCAGGAAGGCTTTGACCATAGGGATAGCAAAGTGTCCCTGCAAGAGAAAAACTGTGAGCCTGTGGTCCCCAATGCCCCTCCCGCT
        : MART
Gene
Segment# : 7
Offset
       : 91
 Q B K N C E P V V P N A P P A Y E K L S A E Q S P F P Y S P
Gene
       : MART
Segment# : 8
Offset
       : 106
1st Codon : 1
 YEKLSAEQSPPPYSPAA
TACGAAAAGCTCAGCGCTGAGCAAAGCCCTCCCCCTTACTCCCCCGCTGCC
        : TRP-1
Gene
Segment# : 1
Offset
       : 1
1st Codon : 1
 A A P A F L T W H R Y H L L R L B K D M Q B M L Q E P S F S
GCCGCTCCCGCTTTCCTCACCTGGCACAGATACCATCTGCTCAGGCTCGAGAAAGACATGCCAGGAAATGCTCCAGGAACCCTCCTTCTCC
Gene
       : TRP-1
Segment# : 2
       : 16
Offset
1st Codon : 1
 L B K D M Q B M L Q E P S P S L P Y W N F A T G K N V C D I
Gene
       : TRP-1
Segment# : 3
Offset
       : 31
1st Codon : 1
 L P Y W N F A T G R N V C D I C T D D L M G S R S N F D S T
CTGCCTTACTGGAACTTTGCCACAGGCAAAAACGTCTGCGATATCTGTACCGATGACCTCATGGGAAGCAGAAGCAATTTCGATAGCACA
Gene
       : TRP-1
Segment# : 4
Offset
       : 46
1st Codon : 1
C T D D L M G S R S N F D S T L I S P N S V F S Q W R V V C
TGCACAGACGATCTGATGGGCTCCAGGTCCAACTTTGACTCCACCCTCATCTCCCCCAATAGCGTCTTCTCCCAGTGGAGGGTCGTGTGT
Gene
       : TRP-1
Segment# : 5
Offset
      : 61
1st Codon : 1
L I S P N S V P S Q W R V V C D S L B D Y D T L G T L C N S
CTGATTAGCCCTAACTCCGTGTTTAGCCAATGGAGAGTGGTCTGCGATAGCCTCGAGGATTACCATCGCGCACACTGTGTAACTCC
Gene
       : TRP-1
Segment# : 6
      : 76
Offset
1st Codon : 1
D S L B D Y D T L G T L C N S T B D G P I R R N P A G N V A
GACTCCCTGGAAGACTATGACACACTGGGAACCCTCTGCAATAGCACAGAGGATGGCCCTATCAGAAGGAATCCCGCTGGCAATGTGGCT
Gene
       : TRP-1
Segment# : 7
Offset
      : 91
T B D G P I R R N P A G N V A R P M V Q R L P B P Q D V A Q
ACCGAAGACGGACCCATTAGGAGAAACCCTGCCGGAAACGTCGCCAGACCCCATGGTGCAAAGGCTCCCCGAACCCCCAAGACGTCGCCCAA
```

#### 157/216 : TRP-1 Segment# : 8 Offset : 106 1st Codon : 1 R P M V Q R L P B P Q D V A Q C L B V G L P D T P P P Y S N AGGCCTATGGTCCAGAGACTGCCTGAGCCTCAGGATGTGGCTCAGTGTCTGGAAGTGGGACTGTTTGACACACCCCCTTTCTATAGCAAT Gene : TRP-1 Segment# : 9 : 121 Offset 1st Codon : 1 C L E V G L F D T P P F Y S N S T N S F R N T V E G Y S D P TGCCTCGAGGTCGGCCTCTTCGATACCCCTCCCTTTTACTCCAACTCCACCAATAGCTTTAGGAATACCGTCGAGGGATACTCCGACCCT Gene : TRP-1 Segment# : 10 Offset : 136 1st Codon : 1 S T N S P R N T V B G Y S D P T G K Y D P A V R S L H N L A AGCACAAACTCCTTCAGAAACACAGTGGAAGGCTATAGCGATCCCACAGGCAAATACGATCCCGCTGTGAGAAGCCTCCACAATCTGGCT Gene : TRP-1 Segment# : 11 Offset : 151 T G K Y D P A V R S L H N L A H L P L N G T G G Q T H L S S Gene : TRP-1 Segment# : 12 Offset : 166 1st Codon : 1 H L F L N G T G G Q T H L S S Q D P I P V L L H T P T D A V CACCTCTTCCTCAACGGAGCCCAAACCCATCTGTCCAGCCAAGACCCTATCTTTGTGCTCCTGCATACCTTTACCGATGCCGTC : TRP-1 Gene Segment# : 13 Offset : 181 1st Codon : 1 Q D P I P V L L H T F T D A V F D E W L R R Y N A D I S T P CAGGATCCCATTTTCGTCCTCCTCCACACATTCACAGACGCTGTGTTTGACGAATGGCTCAGGAGATACAATGCCGATATCTCCACCTTT : TRP-1 Gene Segment# : 14 Offset : 196 1st Codon : 1 P D E W L R R Y N A D I S T P P L B N A P I G H N R O Y N M Gene : TRP-1 Segment# : 15 Offset : 211 1st Codon : 1 P L E N A P I G H N R Q Y N M V P P W P P V T N T E M F V T CCCCTCGAGAATGCCCCCTATCGGACACAATAGGCAATACAATATGGTCCCCTTTTGGCCTCCCGTCACCAATACCGAAATGTTTGTGACA Gene : TRP-1 Segment# : 16 Offset : 226 1st Codon : 1 V P P W P P V T N T E M P V T A P D N L G Y T Y E A A GTGCCTTTCTGGCCCCCTGTGACAACACAGAGATGTTCGTCACCGCTCCCGATAACCTCGGCTATACCTATGAGGCTGCC Gene : Tyros Segment# : 1 Offset : 1 1st Codon : 1 A A M L L A V L Y C L L W S F Q T S A G H P P R A C V S S K

Figure 27 (Cont)

GCCGCTATGCTCCTGGCTGTGCTCTACTGTCTCTGGTCCTTCCAAACCTCCGCCGGACACTTTCCCAGAGCCTGTGTGTCCAGCAAA

Gene

Segment# : 2

: Tyros

# 158/216

Offset 1st Codon : 1 Q T S A G H P P R A C V S S K N L M E K E C C P P N S G D R : Tyros Segment# : 3 Offset : 31 1st Codon : 1 N L M E K B C C P P W S G D R S P C G Q L S G R G S C Q N I AACCTCATGGAAAAGGAATGCTGTCCCCCTTGGTCCGGCGATAGGTCCCCCTGTGGCCAACTGTCCGGCAGAGGCTCCTGCCAAACATT : Tyros Gene Segment# : 4 Offset : 46 1st Codon : 1 S P C G Q L S G R G S C Q N I L L S N A P L G P Q F P F T G AGCCCTTGCGGACAGCTCAGCGGAAGGGGGAAGCTGTCAGAATATCCTCCTGTCCAACGCTCCCTCGGCCCTCAGTTTCCCTTTACCGGA Gene : Tyros Segment# : 5 Offset : 61 1st Codon : 1 LLSNAPLGPQFPFTGVDDRESWPSVFYNRT CTGCTCAGCAATGCCCCTCTGGGACCCCAATTCCCTTTCACAGGCGTCGACGATAGGGAAAGCTGGCCCTCCGTGTTTTACAATAGGACA Gene : Tyros Segment# : 6 : 76 Offset 1st Codon : 1 V D D R B S W P S V P Y N R T C Q C S G N F M G F N C G N C GTGGATGACAGAGAGTCCTGGCCTAGCGTCTTCTATAACAGAACCTGTCAGTGTAGCGGAAACTTTTATGGGATTCAATTGCGGAAACTGT Gene : Tyros Segment# : 7 Offset : 91 1st Codon : 1 C Q C S G N P M G F N C G N C K P G P W G P N C T E R R L L TGCCAATGCTCCGGCAATTTCATGGGCTTTAACTGTGGCAATTGCAAATTCGGATTCTGGGGCCCTAACTGTACCGAAAGGACACTGCTC Gene : Tyros Segment# : 8 Offset : 106 1st Codon : 1 K F G F W G P N C T B R R L L V R R N I F D L S A P B K D K AAGTTTGGCTTTTGGGGACCCAATTGCACAGAGAGAGAGGCTCCTGGTCAGGAGAAACATTTTCGATCTGTCCGCCCCTGAGAAAGACAAA : Tyros Segment# : 9 Offset : 121 1st Codon : 1 V R R N I F D L S A P E K D K F F A Y L T L A K H T I S S D GTGAGAAGGAATATCTTTGACCTCAGCGCTCCCGAAAAGGATAAGTTTTTCGCTTACCTCACCCTCGCCAAACACACAATCTCCAGCGAT Gene : Tyros Segment# : 10 Offset : 136 1st Codon : 1 FFAYLTLAKHTISSDYVIPIGTYGQMKNGS TTCTTTGCCTATCTGACACTGGCTAAGCATACCATTAGCTCCGACTATGTGATTCCCATTGGCACATACGGACAGATGAAGAATGGCTCC Gene : Tyros Segment# : 11 Offset : 151 1st Codon : 1 YVIPIGTYGQMKBGSTPMFNDINIYDLFVW TACGTCATCCCTATCGGAACCTATGGCCAAATGAAAAACCGGAAGCACCCCATGTTCAATGACATTAACATTTACGATCTGTTTGTGTGG Gene : Tyros Segment# : 12 Offset : 166 1st Codon : 1

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T P M F N D I N I Y D L F V N M H Y Y V S M D A L L G G S E ACCCCTATGTTTAACGATATCAATATCTATGACCTCTTCGTCTGGATGCACCTATTACGTCAGCATGGACGCTCTGCTCGGCGGAAGCGAA : Tyros Segment# : 13 Offset : 181 1st Codon : 1 M H Y Y V S M D A L L G G S E I W R D I D P A H E A P A F L ATGCATTACTATGTGTCCATGGATGCCCTCCTGGGAGGCTCCGAGATTTGGAGAGACATTGACTTTGCCCATGAGGCTCCCGCTTTCCTC Gene : Tyros Segment# : 14 : 196 Offset 1st Codon : 1 I W R D I D F A H E A P A F L P W H R L F L L R W E Q E I Q ATCTGGAGGGATATCGATTTCGCTCACGAAGCCCCTGCCTTTCTGCCTTGGCATAGGCTCTTCCTCCTGAGATGGGAACAGGAAATCCAA Gene : Tyros Segment# : 15 Offset : 211 lat Codon : 1 PWHRLFLLRWEQEIQKLTGDENFTIPYWDW  ${\tt CCCTGGCACAGACTGTTTCTGCTCAGGTGGGAGCAAGAGATTCAGAAACTGACAGGCGATGAGAATTTCACAATCCCTTACTGGGACTGG}$ Gene : Tyros Segment# : 16 Offset : 226 1st Codon : 1 K L T G D E N F T I P Y W D W R D A E K C D I C T D E Y M G AAGCTCACCGGAGACGAAAACTTTACCATTCCCTATTGGGATTGGAGAGACGCTGAGAAATGCGATATCTGTACCGATGAGTATATGGGA Gene : Tyros Segment# : 17 Offset : 241 1st Codon : 1 RDAEKCDICTDBYMGGQHPTNPNLLSPASP AGGGATGCCGAAAAGTGTGACATTTGCACAGACGAATACATGGGCGGACAGCATCCCACAAACCCTAACCTCCTGTCCCCCGGTAGCTTT Gene : Tvros Segment# : 18 Offset : 256 1st Codon : 1 G Q H P T N P N L L S P A S F F S S W Q I V C S R L R B Y N GGCCAACACCCTACCAATCCCAATCTGCTCAGCCCTGCCTCCTTCTTTAGCTCCTGGCAAATCGTCTGCTCCAGGCTCGAGGAATACAAT Gene : Tyros Segment# : 19 : 271 Offset 1st Codon : 1 PSSWQIVCSRLBBYNSHQSLCNGTPBGPLR TTCTCCAGCTGGCAGATTGTGTAGCAGACTGGAAGAGTATAACTCCCACCAAAGCCTCTGCAATGGCACACCCGAAGGCCCTCTGAGA Gene : Tyros Segment# : 20 Offset : 286 1st Codon : 1 S H Q S L C N G T P B G P L R R N P G N H D K S R T P R L P AGCCATCAGTCCCTGTGTAACGGAACCCCTGAGGGACCCCTCAGGAGAAACCCTGGCAATCACGATAAGTCCAGGACACCCCAGACTGCCT Gene : Tyros Segment# : 21 Offset : 301 1st Codon : 1 RNPGNHDKSRTPRLPSSADVEFCLSLTQYE AGGAATCCCGGAAACCATGACAAAAGCAGAACCCCTAGGCTCCCCTCCAGCGCTGACGTCGAGTTTTGCCTCAGCCTCACCCAATACGAA Gene : Tyros Segment# : 22 Offset : 316 1st Codon : 1 S S A D V E P C L S L T Q Y E S G S M D K A A N P S P R N T AGCTCCGCCGATGTGGAATTCTGTCTGTCCCTGACACAGTATGAGTCCGGCTCCATGGATAAGGCTGCCAATTTCTCCTTCAGAAACACA

# 160/216

Gene : Tyros Segment# : 23 Offset : 331 1st Codon : 1 S G S M D K A A N P S P R N T L E G P A S P L T G I A D A S AGCGGAAGCATGGACAAAGCCGCTAACTTTAGCTTTAGGAATACCCTCGAGGGGATTCGCTAGCCCTCTGACAGGCATTGCCGATGCCTCC Gene : Tyros Segment# : 24 Offset : 346 1st Codon : 1 L B G F A S P L T G I A D A S Q S S M H N A L H I Y M N G T  $\tt CTGGAAGGCTTTGCCTCCCCCTCACCGGAATCGCTGACGCTAGCCAAAGCTCCATGCATAACGCTCTGCATATCTATATGAATGGCACA$ Gene : Tyros Segment# : 25 Offset : 361 1st Codon : 1 Q S S M H N A L H I Y M N G T M S Q V Q G S A N D P I F L L CAGTCCAGCATGCACAATGCCCTCCACATTTACATGAACGGAACCATGAGCCAAGTGCAAGGCTCCGCCAATGACCCTATCTTTCTGCTC Gene : Tyros Segment# : 26 : 376 1st Codon : 1 M S Q V Q G S A N D P I F L L H H A F V D S I F E Q W L Q R ATGTCCCAGGTCCAGGGAAGCGCTAACGATCCCATTTTCCTCCTGCATCACGCTTTCGTCGACTCCATCTTTGAGCAATGGCTCCAGAGA Gene : Tyros Segment# : 27 Offset : 391 1st Codon : 1 H H A F V D S I F E Q W L Q R H R P L Q E V Y P E A N A P I CACCATGCCTTTGTGGATAGCATTTTCGAACAGTGGCTGCAAAGGCATAGGCCTCTGCAAGAGGTCTACCCTGAGGCTAACGCTCCCATT Gene : Tyros Segment# : 28 Offset : 406 1st Codon : 1 HRPLQEVYPEANAPIGHNRESYMVPPIPLY CACAGACCCCTCCAGGAAGTGTATCCCGAAGCCAATGCCCCTATCGGACACAATAGGGAAAGCTATATGGTCCCCTTTATCCCTCTGTAT Gene : Tyros Segment# : 29 Offset : 421 1st Codon : 1 G H N R B S Y M V P F I P L Y R N G D P F I S S K D L G Y D GGCCATAACAGAGAGTCCTACATGGTGCCTTTCATTCCCCTCTACAGAAACGGAGACTTTTTCATTAGCTCCAAGGATCTGGGATACGAT : Tyros Gene Segment# : 30 Offset : 436 1st Codon : 1 RNGDPFISSKDLGYDYSYLQDSDPDSFQDY AGGANTGGCGATTTCTTTATCTCCAGCAAAGACCTCGGCTATGACTATAGCTATCTGCAAGACTCCGACCCTGACTCCTTCCAAGACTAT Cene : Tyros Segment# : 31 : 451 1st Codon : 1 Y S Y L Q D S D P D S P Q D Y I K S Y L B Q A S R I W S W L TACTCCTACCTCCAGGATAGCGATCCCGATAGCTTTCAGGATTACATTAAGTCCTACCTCGAGCAAGCCTCCAGGATTTGGTCCTGGCTC Gene : Tyros Segment# : 32 Offset : 466 1st Codon : 1 I K S Y L E Q A S R I W S W L L G A A M V G A V L T A L L A Gene : Tyros

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Segment# : 33 Offset : 481 1st Codon : 1 LGAAMVGAVLTALLAGLVSLLCRHKRKQLP CTGGGAGCCGCTATGGTCGGCGCTGTGCTCACCGCTCTGCTCGCCGGACTGGTCAGCCTCCTGTGTAGGCATAAGAGAAAGCAACTGCCT : Tyros Segment# : 34 Offset : 496 1st Codon : 1 G L V S L L C R H K R K Q L P E E K Q P L L M E K B D Y H S GGCCTCGTGTCCCTGCTCTGCAGACACAAAAGGAAACAGCTCCCCGAAGAGAAACAGCCTCTGCTCATGGAAAAGGAAGACTATCACTCC Gene : Tyros Segment# : 35 Offset : 511 1st Codon : 1 EBKQPLLMEKEDYHSLYQSHLAA GAGGAAAAGCAACCCCTCCTGATGGAGAAAGAGGGATTACCATAGCCTCTACCAAAGCCATCTGGCTGCC Gene : TRP2 Segment# : 1 Offset 1st Codon : 1 A A M S P L W W G P L L S C L G C K I L P G A Q G Q P P R V GCCGCTATGTCCCCCCTCTGGTGGGGCTTTCTGCTCAGCTGTCTGGGATGCAAAATCCTCCCCGGAGCCCAAGGCCAATTCCCTAGGGTC Gene : TRP2 Segment# : 2 Offset : 16 1st Codon : 1 G C K I L P G A Q G Q F P R V C M T V D S L V N K E C C P R GGCTGTAAGATTCTGCCTGGCGCTCAGGGACAGTTTCCCAGAGTGTGTATGACAGTGGATAGCCTCGTGAATAAGGAATGCTGTCCCAGA Gene : TRP2 Segment# : 3 Offset : 31 C M T V D S L V N K E C C P R L G A E S A N V C G S Q Q G R Gene : TRP2 Segment# : 4 Offset : 46 1st Codon : 1 L G A B S A N V C G S Q Q G R G Q C T B V R A D T R P W S G CTGGGAGCCGAAAGCGCTAACGTCTGCGGAAGCCAACAGGGAAGCGGACAGTGTACCGAAGTGAGAGCCGATACCAGACCCTGGAGCGGA : TRP2 Gene Segment# : 5 Offset : 61 1st Codon : 1 G Q C T E V R A D T R P W S G P Y I L R N Q D D R E L W P R GGCCAATGCACAGAGGTCAGGGCTGACACAAGGCCTTGGTCCGGCCCTTACATTCTGAGAAAACCAAGACGATAGGGAACTGTGGCCCAGA : TRP2 Gene Segment# : 6 : 76 Offset 1st Codon : 1 PYILRNQDDRELWPRKPPHRTCKCTGNFAG CCCTATATCCTCAGGAATCAGGATGACAGAGAGCTCTGGCCTAGGAAATTCTTTCACAGAACCTGTAAGTGTACCGGAAACTTTGCCGGA : TRP2 Gene Segment# : 7 K F F H R T C K C T G N F A G Y N C G D C K F G W T G P N C AAGTTTTTCCATAGGACATGCAAATGCACAGGCAATTTCGCTGGCTATAACTGTGGCGATTGCAAATTCGGATGGACAGGCCCTAACTGT : TRP2 Segment# : 8

Figure 27 (Cont)

Offset

: 106

# 162/216

1st Codon : 1 YNCGDCKPGWTGPNCERKKPPVIRQNIHSL Gene : TRP2 Segment# : 9 : 121 1st Codon : 1 ERKKPPVIRQNIHSLSPQEREQPLGALDLA : TRP2 Segment# : 10 Offset : 136 1st Codon: 1
S P Q E R E Q F L G A L D L A K K R V H P D Y V I T T Q H W AGCCCTCAGGAAAGGGAACAGTTTCTGGGAGCCCTCGACCTCGCCAAAAAGAGAGTGCATCCCGATTACGTCATCACAACCCCAACACTGG : TRP2 Segment# : 11 Offset : 151 1st Codon : 1 K K R V H P D Y V I T T Q H W L G L L G P N G T Q P Q F A N AAGAAAAGGTCCACCTGACTATGTGATTACCACACAGCATTGGCTCGGCCTCCTGGGACCCAATGGCACACAGCCTCAGTTTGCCAAT Gene : TRP2 Segment# : 12 Offset : 166 1st Codon : 1 L G L L G P N G T Q P Q F A N C S V Y D F P V W L H Y Y S V CTGGGACTGCTCGGCCCTAACGGAACCCCAACTCGCTAACTGTAGCGTCTACGATTTCTTTGTGTGGCTGCATTACTATAGCGTC Gene Segment# : 13 Offset : 181 1st Codon : 1 C S V Y D F F V W L H Y Y S V R D T L L G P G R P Y R A I D TGCTCCGTGTATGACTTTTTCGTCTGGCTCCACTATTACTCCGTGAGAGACACACTGCTCGGCCAGGACCCTATAGGGCTATCGAT Gene Segment# : 14 Offset : 196 1st Codon : 1 R D T L L G P G R P Y R A I D F S H Q G P A P V T W H R Y H AGGGATACCCTCCTGGGACCCGGAAGGCCTTACAGAGCCATTGACTTTAGCCATCAGGGACCCGCTTTCGTCACCTGGCACAGATACCAT : TRP2 Segment# : 15 : 211 Offset 1st Codon : 1 PSHQGPAPVT WHRYHLLCLERDLQRLIGNE TTCTCCCACCAAGGCCCTGCCTTTGTGACATGGCATAGGTATCACCTCCTGTGTCTGGAAAGGGATCTGCAAAGGCTCATCGGAAACGAA : TRP2 Segment# : 16 Offset : 226 1st Codon : 1 L L C L B R D L Q R L I G N E S F A L P Y W N F A T G R N E CTGCTCTGCCTCGAGAGAGACCTCCAGAGACTGATTGGCAATGAGTCCTTCGCTCTGCCTTACTGGAAACTTTGCCACAGGCAGAAACGAA Gene : TRP2 Segment# : 17 Offset : 241 1st Codon : 1 S F A L P Y W N F A T G R N E C D V C T D Q L F G A A R P D : TRP2 Gene Segment# : 18 Offset : 256 1st Codon : 1 C D V C T D Q L P G A A R P D D P T L I S R N S R P S S W R

# 163/216

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TGCGATGTGTGTACCGATCAGCTCTTCGGAGCCGCTAGGCCTGACGATCCCACACTGATTAGCAGAAACTCCAGGTTTAGCTCCTGGGAA
        : TRP2
 Segment# : 19
 Offset
       : 271
 1st Codon : 1
 D P T L I S R N S R F S S W E T V C D S L D D Y N H L V T L
 GACCCTACCCTCATCTCCAGGAATAGCAGATTCTCCAGCTGGGAGACAGTGTGTGACTCCCTGGATGACTATAACCATCTGGTCACCCTC
 Gene
        : TRP2
 Segment# : 20
        : 286
 Offset
 TVCDSLDDYNHLVTLCNGTYEGLLRRNQMG
 ACCGTCTGCGATAGCCTCGACGATTACAATCACCTCGTGACACTGTGTAACGGAACCTATGAGGGACTGCTCAGGAGAAACCAAATGGGA
Gene
        : TRP2
Segment# : 21
Offset
1st Codon : 1
 C N G T Y E G L L R R N Q M G R N S M K L P T L K D I R D C
TGCAATGGCACATACGAAGGCCTCCTGAGAAGGAATCAGATGGGCAGAAACTCCATGAAACTGCCTACCCTCAAGGATATCAGAGACTGT
        : TRP2
Gene
Segment# : 22
Offset
       : 316
1st Codon : 1
 RNSMKLPTLKDIRDCLSLQKPDNPPFPQNS
Gene
       : TRP2
Segment# : 23
Offset
       : 331
1st Codon : 1
 LSLQKPDNPPPPQNSTFSFRNALEGFDKAD
CTGTCCCTGCAAAAGTTTGACAATCCCCCTTTCTTTCAGAATAGCACATTCTCCTTCAGAAACGCTCTGGAAGGCTTTGACAAAGCCGAT
Gene
        : TRP2
Segment# : 24
Offset
       : 346
1st Codon : 1
 T F S F R N A L E G F D K A D G T L D S Q V M S L H N L V H
ACCTTTAGCTTTAGGAATGCCCTCGAGGGATTCGATAAGGCTGACGGAACCCTCGACTCCCAGGTCATGTCCCTGCATAACCTCGTGCAT
Gene
       : TRP2
Segment# : 25
Offset
       : 361
1st Codon : 1
 G T L D S Q V M S L H N L V H S F L N G T N A L P H S A A N
Gene
       : TRP2
Segment# : 26
       : 376
Offset
1st Codon : 1
S F L N G T N A L P H S A A N D P I F V V L H S F T D A I F
AGCTTTCTGAATGGCACAAACGCTCTGCCTCACTCCGCCGCTAACGATCCCATTTTCGTCGTGCTCCACTCCTTCACAGACGCTATCTTT
Gene : TRP2
Segment# : 27
Offset
       : 391
1st Codon : 1
D P I P V V L H S P T D A I P D B W M K R P N P P A D A W P
GACCCTATCTTTGTGGTCCTGCATAGCTTTACCGATGCCATTTTCGATGAGTGGATGAAAAGGTTTAACCCTCCCGCTGACGCTTGGCCT
       : TRP2
Gene
Segment# : 28
1st Codon : 1
DEWNKRPNPPADAWPQELAPIGHNRMYNMV
CACGAATGGATGAAGAGATTCAATCCCCCTGCCGATGCCTGGCCCCCAAGAGCTCGCCCCTATCGGACACAATAGGATGTACAATATGGTC
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Gene : TRP2 Segment# : 29 Offset : 421 1st Codon : 1 Q E L A P I G H N R M Y N M V P F F P P V T N E E L F L T S : TRP2 Gene Segment# : 30 Offset : 436 1st Codon : 1 P P P P V T N E E L F L T S D Q L G Y S Y A I D L P V S V Gene : TRP2 Segment# : 31 Offset : 451 1st Codon : 1 ·D Q L G Y S Y A I D L P V S V E E T P G W P T T L L V V M G GACCAACTGGGATACTCCTACGCTATCGATCTGCCTGTGTCCCGTGGAAGAGACACCCCGGATGGCCTACCACACTGCTCGTCGTCATGGGA : TRP2 Gene Segment# : 32 Offset : 466 E E T P G W P T T L L V V M G T L V A L V G L F V L L A F L GAGGAAACCCCTGGCTGGCCCACAACCCTCCTGGTCGTCGTCGCACACTGGTCGCCCTCGTGGGACTGTTTGTGCTCCTGGCTTTCCTC Gene : TRP2 Segment# : 33 : 481 Offset 1st Codon : 1 T L V A L V G L F V L L A F L Q Y R R L R K G Y T P L M E T ACCCTCGTGGCTCTGGTCGGCCTCTTCGTCCTGCTCGCCTTTCTGCAATACAGAAGGCTCAGGAAAGGCTATACCCCTCTGATGGAGACA : TRP2 Gene Segment# : 34 : 496 Offset 1st Codon : 1 Q Y R R L R K G Y T P L M E T H L S S K R Y T E E A A A CAGTATAGGAGACTGAGAAAGGGATACACCCCTCATGGAAACCCCATCTGTCCAGCAAAAGGTATACCGAAGAGGGCTGCCGCT Gene : MC1R Segment# : 1 Offset : 1 1st Codon : 1 A A M A V Q G S Q R R L L G S L N S T P T A I P Q L G L A A GCCGCTATGGCTGTGCAAGGCTCCCAGAGAAGGCTCCTGGGAAGCCTCAACTCCACCCCTACCGCTATCCCTCAGCTCCGCCTTGCCTCT : MC1R Gene Segment# : 2 : 16 Offset 1st Codon : 1 L N S T P T A I P Q L G L A A N Q T G A R C L B V S I S D G CTGAATAGCACACCCACAGCCATTCCCCAACTGGGACTGGCTGCCAATCAGACAGGCGCTAGGTGTCTGGAAGTGTCCATCTCCCAACGGA Gene : MCIR Segment# : 3 : 31 Offset 1st Codon : 1 NQTGARCLEVSISDGLFLSLGLVSLVENAL AACCAAACCGGAGCCAGATGCCTCGAGGTCAGCATTAGCGATGGCCTCTTCCTCAGCCTCGGCCTCGTGTCCCTGGAGAATGCCCTC Gene : MC1R Segment# : 4 Offset : 46 1st Codon : 1 LPLSLGLVSLVENALVVATIAKNRNLHSPM CTGTTTCTGTCCCTGGGACTGGTCAGCCTCGTGGAAAACGCTCTGGTCGTCGTCGCTACCATTGCCAAAAACAGAAACCTCCACTCCCCCATG

Figure 27 (Cont)

Gene

Segment# : 5

: MC1R

# 165/216

Offset : 61 1st Codon : 1 V V A T I A K N R N L H S P M Y C F I C C L A L S D L L V S GTGGTCGCCACAATCGCTAAGAATAGGAATCTGCATAGCCCTATGTATTGCTTTATCTGTTGCCTCGCCCTCAGCGATCTGCTCGTGTCC Gene : MC1R Segment# : 6 : 76 Offset lat Codon : 1 Y C F I C C L A L S D L L V S G T N V L E T A V I L L E A TACTGTTTCATTTGCTGTCTGGCTCTGGCCCCCGGTCAGCGGAACCAATGTGCTCGAGACAGCCGTCATCCTCCTGCTCGAGGCCT : MC1R Gene Segment# : 7 Offset : 91 1st Codon : 1 G T N V L E T A V I L L E A G A L V A R A A V L O O L D N GGCACAAACGTCCTGGAAACCGCTGTGATTCTGCTCCTGGAAGCCGGAGCCCTCGTGGCTAGGGCTGCCGTCCTGCAACAGCTCGACAAT Gene : MC1R Segment# : 8 Offset : 106 G A L V A R A A V L Q Q L D N V I D V I T C S S M L S S L C GGGGTCTGGTCGCCAGAGCCGCTGTGCTCCAGCAACTGGATAACGTCATCGATGTGATTACCTGTAGCTCCATGCTCAGCTCCCTGTGT Gene : MC1R Segment# : 9 Offset : 121 1st Codon : 1 V I D V I T C S S M L S S L C F L G A I A V D R Y I S I F Y GTGATTGACGTCATCACATGCTCCAGCATGCTGTCCAGCCTCTGCTTTCTGGGAGCCATTGCCGTCGACAGATACATTAGCATTTTTTAT Gene : MC1R Segment# : 10 : 136 Offset 1st Codon : 1 P L G A I A V D R Y I S I F Y A L R Y H S I V T L P R A P R TTCCTCGGCGCTATCGCTGTGGATAGGTATATCTCCATCTTTTACGCTCTGAGATACCATAGCATTGTGACACTGCCTAGGGCTCCCAGA Gene : MC1R Segment# : 11 Offset : 151 1st Codon : 1 A L R Y H S I V T L P R A P R A V A A I W V A S V V F S T L GCCCTCAGGTATCACTCCATCGTCACCCTCCCCAGAGCCCCTAGGGCTGTGGCTGTCGATTTGGGTCGCCTCCGTGGTCTTCTCCACCCTC Gene : MC1R Segment# : 12 Offset : 166 1st Codon : 1 A V A A I W V A S V V F S T L F I A Y Y D H V A V L L C L V GCCGTCGCCGCTATCTGGGTCGCCTAGCGTCGTGTTTAGCACACTGTTTATCGCTTACTATCACCATGTGGCTCTGGTCTCTGGTC : MC1R Gene Segment# : 13 Offset : 181 PIAYYDH VAVLLCLVVFFLAMLVLMAVLYV TTCATTGCCTATTACGATCACGTCGCCGTCCTGCTCTCCTCGTGGTCTTCTTCTGGCTATGCTCGTGCTCATGGCTGTGCTCTACGTC Gene : MC1R Segment# : 14 Offset : 196 V P P L A M L V L M A V L Y V H M L A R A C Q H A Q G I A R GTGTTTTTCCTCGCCATGCTGGTCCTGATGGCCGTCCTGTATGTGCATATGCTCGCCAGGGCCTGTCAGCATGCCCAAGGCATTGCCAGA : MClR Gene Segment# : 15 : 211 Offset 1st Codon: 1

Figure 27 (Cont)

# 166/216

H M L A R A C Q H A Q G I A R L H K R Q R P V H Q G F G L K CACATGCTGGCTAGGGCTTGCCAACACGCTCAGGGAATCGCTAGGCTCCACAAAAGGCAAAGGCCTGTGCATCAGGGATTCGGACTGAAA : MC1R Gene Segment# : 16 Offset : 226 1st Codon : 1 LHKRQRPVHQGPGLKGAVTLTILLGIPPLC : MC1R Segment# : 17 Offset : 241 1st Codon : 1 G A V T L T I L L G I P P L C W G P P P L H L T L I V L C P Gene : MC1R Segment# : 18 Offset : 256 1st Codon : 1 W G P P P L H L T L I V L C P E H P T C G C I P K N P N L P TGGGGACCCTTTTTCCTCCACCTCACCCTCATCGTCCTGTGTCCCGAACACCCTACCTGTGGCTGTATCTTTAAGAATTTCAATCTGTTT Gene Segment# : 19 Offset : 271 1st Codon : 1 E H P T C G C I F K N F N L F L A L I I C N A I I D P L I Y GAGCATCCCACATGCGGATGCATTTTCAAAAACTTTAACCTCTTCCTCGCCCTCATCATCTTGCAATGCCATTATCGATCCCCTCATCTAT : MC1R Segment# : 20 Offset : 286 1st Codon : 1 LALIICNAIIDPLIYAFHSQELRRTLKEVL CTGGCTCTGATTATCTGTAACGCTATCATTGACCCTCTGATTTACGCTTTCCATAGCCAAGAGCCTCAGGAGAACCCTCAAGGAAGTGCTC Segment# : 21 Offset : 301 1st Codon : 1 AFHSOBLRRTLKEVLTCSWAA GCCTTCACTCCCAGGAACTGAGAAGGACACTGAAAAGAGGTCCTGACATGCTCCTGGGCTGCC : MUC1F Gene Segment# : 1 Offset : 1 1st Codon : 1 A A M T P G T Q S P P P L L L L T V L T V V T G S G H A S GCCGCTATGACACCCGGAACCCAAAGCCCTTTCTTTCTGCTCCTGCTCCTGACAGTGCTCACCGTCGTGACAGGCTCCCGCCCATGCCTCC Gene : MUCLP Segment# : 2 Offset : 16 1st Codon : 1 L L T V L T V V T G S G H A S S T P G G E K E T S A T Q R S CTGCTCACCGTCCTGACAGTGGTCACCGGAAGCGGACACGCTAGCTCCACCCCTGGCGGAGAGAAGAGACAAGCGCTACCCAAAGGTCC : MUCLP Gene Segment# : 3 Offset : 31 1st Codon : 1 STPGGEKETSATQRSSVPSSTEKNAVSMTS AGCACACCGGAGGGGAAAAGGAAACCTCCGCCACACAGAGAAGCTCCGTGCCTAGCTCCACCGAAAAGAATGCCGTCAGCATGACCTCC : MUC1F Gene Segment# : 4 Offset : 46 1st Codon : 1 S V P S S T B K N A V S M T S S V L S S H S P G S G S S T T AGCGTCCCTCCAGCACAGAGAAAAACGCTGTGTCCATGACAAGCTCCGTGCTCAGCTCCCACTCCCCGGAAGCGGAAGCTCCACCACA

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: MUC1F Gene Segment# : 5 : 61 Offset 1st Codon : 1 S V L S S H S P G S G S S T T Q G Q D V T L A P A T B P A S Gene : MUC1F Segment# : 6 : 76 Offset 1st Codon : 1 Q G Q D V T L A P A T E P A S G S A A T W G Q D V T S V P V CAGGGACAGGATGTGACACTGGCTCCCGCTACCGGAACCCGCTAGCGGAAGCGCTGCCACATGGGGACAGGATGTGACAAGCGTCCCCGTC Gene : MUC1F Segment# : 7 Offset : 91 1st Codon : 1 G S A A T W G Q D V T S V P V T R P A L G S T T P P A H D V Segment# : 8 : 106 1st Codon : 1 T R P A L G S T T P P A H D V T S A P D N K A A ACCAGACCGGTCTGGGAAGCACAACCCCTCCCGGTCACGATGTGACAAGCGGTCCCGATAACAAAGCCGCT Gene : MUC1R Segment# : 1 Offset : 1 1st Codon : 1 A A N R P A L G S T A P P V H N V T S A S G S A S G S A S T GCCGCTAACAGACCCGCTCTGGGAAGCACAGCCCCTCCCGTCCACAATGTGACAAGCGCTAGCGGAAGCGCTAGCGGAAGCGCTAGCACA Gene : MUC1R Segment# : 2 Offset : 16 1st Codon : 1 N V T S A S G S A S G S A S T L V H N G T S A R A T T T P A Gene : MUC1R Segment# : 3 Offset : 31 1st Codon : 1 LVHNGTSARATTTPASKSTPFSIPSHHSDT CTGGTCCACAATGGCACAAGCGCTAGGGCTACCACACCCCTGCCTCCAAGTCCACCCCTTTCTCCATCCCTAGCCATCACTCCGACACA Gene : MUC1R Segment# : 4 : 46 Offset 1st Codon : 1 S K S T P P S I P S H H S D T P T T L A S H S T K T D A S S : MUC1R Gene Segment# : 5 Offset : 61 PTTLASHST KTDASSTHHSS V PPLTS S N H S  $\tt CCCACAACCCTCGCCTCCCACTCCACCAAAACCGATGCCTCCAGCACACCACTAGCTCCCTCACCTCACCTCAGCAATCACTCC$ : MUC1R Gene Segment# : 6 : 76 Offset THHSSVPPLTSSNHSTSPQLSTGVSPPPLS Gene : MUCIR

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Segment# : 7 Offset : 91 1st Codon : 1

T S P Q L S T G V S P F F L S P H I S N L Q F N S S L B D P ACCTCCCCCAACTGCCACCGGAGTGCCCTCTTTTTTCCTCAGCTTTCACATTAGCAATCTGCAATTCAATAGCTCCCTGGAAGACCCT

Gene : MUCIR Segment# : 8 Offset : 106 1st Codon : 1

F H I S N L Q F N S S L E D P S T D Y Y Q E L Q R D I S E M
TTCCATATCTCCAACCTCCAGCTTTAACTCCAGCCTCCAGCGATCCTCCACCGATTACTATCAGGAACTGCAAAGGGATATCTCCGAGGATG

Gene : MUC1R Segment# : 9 Offset : 121 1st Codon : 1

S T D Y Y Q E L Q R D I S E M F L Q I Y K Q G G F L G L S N AGCACAGACTATTACCAAGAGCTCCAGAGAGACATTAGCGAAATGTTTCTGCAAATCTATAAGCAAGAGCGGATTCCTCGGCCTCAGCAAT

Gene : MUC1R Segment# : 10 Offset : 136 1st Codon : 1

PLQIYKQGGPLGLSNIKFRPGSVVVQLTLA

Gene : MUCIR
Segment# : 11
Offset : 151
1st Codon : 1

Gene : MUC1R Segment# : 12 Offset : 166 1st Codon : 1

FREGTINVHDVETQFNQYKTEAASSRYNLTITCAGGGAACCCACTTCAATCAGTATAAGACGAGGCTGCCTCCAGGTATAACCTCACCATT

Gene : MUC1R
Segment# : 13
Offset : 181
1st Codon : 1

N Q Y K T E A A S R Y N L T I S D V S V S D V P P P P S A Q AACCAATACAAACCGAAGCCGCGAGATACAATCTGACAATCTCGACGACGTCAGCGTCAGCGATGTGCCTTTCCCCTTTCTCCGCCCAA

Gene : MUCIR Segment# : 14 Offset : 196 1st Codon : 1

S D V S V S D V P P P P S A Q S G A G V P G W G I A L L V L AGGGATGTGTCCGGATGCGCGTCCCCGGTTCCCTTTAGCGCTCAGTCCGGCGCTCCCCGGATGGGGAATCGCTCTGCTCGTGCTC

Gene : MUC1R Segment# : 15 Offset : 211 1st Codon : 1

S G A G V P G W G I A L L V L V C V L V A L A I V Y L I A L AGCGGAGCCGGAGTGCCTGGCGATTGCCCTCCTGGTCCTGGTCCTGGTCCTGGTCCTGGCCATTGTTATCTGATTGCCCTC

Gene : MUC1R Segment# : 16 Offset : 226 1st Codon : 1

Gene : MUC1R Segment# : 17 Offset : 241

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1st Codon : 1

AVCQCRRKNYGQLDIFPARDTYHPMSBYPT GCCGTCTGCCAATGCAGAAGGAAAAACTATGGCCAACTGGATATCTTTCCCGCTAGGGATACCTATCACCCTATGTCCGAGTATCCCACA

Gene : MUC1R Segment# : 18 Offset : 256 1st Codon : 1

FPARDTY HPMSBYPTY HTHGRY VPPSSTDR 

: MUC1R Segment# : 19 Offset : 271 lst Codon : 1

Y H T H G R Y V P P S S T D R S P Y E K V S A G N G G S S L TACCATACCCATGGCAGATACGTCCCCCTAGCTCCACCGATAGGTCCCCCTATGAGAAAGTGTCCGCCGGAAACGGAGGCTCCAGCCTC

Gene : MUC1R Segment# : 20 Offset : 286 1st Codon : 1

SPYBK V SAGNGG SSL SYTNPAVAAA SAN LA AGCCCTTACGAAAAGGTCAGCGCTGGCAATGGCGGAAGCTCCCTGTCCTACACAAACCCTGCCGTCGCCGCTGCCTCCGCCAATCTGGCT

Gene : MUC1R Segment# : 21 Offset : 301 1st Codon : 1

SYTNPAVAAASANLAA AGCTATACCAATCCCGCTGTGGCTGCCGCTAGCGCTAACCTCGCCGCT

Segments in scrambled order:

qp100 #4

WNRQLYPEWTEAQRLDCWRGGQVSLKVSND TGGAATAGGCAACTGTATCCCGAATGGACAGAGGCTCAGAGACTGGATTGCTGGAGGGGGAGGCCAAGTGTCCCTGAAAGTGTCCAACGAT

PYILRNQ DDRELWPRKFFHRTCKCTGNFAG CCCTATATCCTCAGGAATCAGGATGACAGAGAGGCTCTGGCCTAGGAAATTCTTTCACAGAACCTGTAAGTGTACCGGAAACTTTGCCGGA

RNGDPFISSRDLGYDYSYLQDSDPDSFQDY AGGAATGGCGATTTCTTTATCTCCAGCAAAGACCTCGGCTATGACTATAGCTATCTGCAAGACTCCGACCCTGACCTCTTCCAAGACTAT

A A P A F L T W H R Y H L L R L E K D M Q E M L Q E P S F S GCCGCTCCCGCTTTCCTCACCTGGCACAGATACCATCTGCTCAGGCTCGAGAAAGACATGCAGGAAATGCTCCAGGAACCCTCCTTCTCC

Tyros #29

G H N R E S Y M V P F I P L Y R N G D F F I S S K D L G Y D GGCCATAACAGAGAGTCCTACATGGTGCCTTTCATTCCCCTCTACAGAAACGGAGACTTTTTCATTAGCTCCAAGGATCTGGGATACGAT

L L C L B R D L Q R L I G N B S P A L P Y W N P A T G R N B CTGCTCTGCCTCGAGAGACCCTCCAGAGACTGATTGGCAATGAGTCCTTCGCTCTGCCTTACTGGAACTTTGCCACAGGCAGAAACGAA

gp100 #23

T T B V V G T T P G Q A P T A B P S G T T S V Q V P T T B V ACCACAGAGGTCGTGGGAACCACACCCGGACAGCCTCCCACAGCCGGACCCTCCGGCACACCTCCGTGCAACTGCCTACCACAGAGGTC

MUC1R #9

STDYYQELQRDISEMFLQIYKQGGFLGLSN AGCACAGACTATTACCAAGAGCTCCAGAGAGACATTAGCGAAATGTTTCTGCAAATCTATAAGCAAGGCGGATTCCTCGGCCTCAGCAAT

A C M B I S S P G C Q P P A Q R L C Q P V L P S P A C Q L V 

TRP2 #31

D Q L G Y S Y A I D L P V · S V E E T P G W P T T L L V V M G

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GACCAACTGGGATACTCCTACGCTATCGATCTGCCTGTGTCCGTGGAAGAGACACCCGGATGGCCTACCACACTGCTCGTGGTCATGGGA

TRP-1 #7

T E D G P I R R N P A G N V A R P M V Q R L P E P Q D V A Q ACCGAAGACGCCATTAGGAGAACCCTGCCGGAAACGTCGCCAGACCCATGGTGGAAACGCTCGCCGAACCCCAAGACGTCGCCAA

TRP2 #3

MUC1R #13

N Q Y K T B A A S R Y N L T I S D V S V S D V P P P F S A Q AACCAATACAAACCGAAGCCGCTAGCAGATACAATCTCGACCATCTCCGACGTCAGCGTCAGCGATGTGCCTTTCCCTTTCTCCGCCCAA

TRP2 #1

A A M S P L W W G F L L S C L G C K I L P G A Q G Q F P R V GCCGCTATGTCCCCCGTGGGGGCCTTTCTGCTCAGCTGTCTCGGATGCAAAATCCTCCCCGGAGCCCAAGGCCAATTCCCTAGGGTC

gp100 #18

qp100 #27

MUC1R #11

MUCLF #7

G S A A T W G Q D V T S V P V T R P A L G S T T P P A H D V GGCTCCGCCCTACCTCGCCCAAGACGTCACCTCCGTGCCTGTGACAAGGCCTGCCCTCGGCTCCACCACCCCCTGCCCATGACGTC

MCIR #16

MC1R #20

L A L I I C N A I I D P L I Y A F H S Q E L R R T L K E V L CTGGCTCTGATTATCGCTATCATCATCATCATCACCATTCACCAGAGCTCAGGAGACCCTCAAGGAACCCTCAAGGAACTGCTC

TRP2 #7

TRP2 #23

LSLQKPDNPPPPQNSTPSPRNALEGFDKAD CTGTCCCTGCAAAAGTTTGACAATCCCCCTTTCTTCAGAATAGCACATTCTCCTTCAGAAACGCTCTGGAAGGCTTTGACAAAGCCGAT

MUC1R #4

MUCIR #1

A A N R P A L G S T A P P V H N V T S A S G S A S G S A S T GCCGCTAACAGCCCCTCCGGCACACCACAATGTGACAAGCGCTAGCGGAAGCGCTAGCGCAAGCGCTAGCACAC

TRP2 #21

C N G T Y E G L L R R N Q M G R N S M K L P T L K D I R D C TGCAATGGCACATACGAAGGCCTCCTGAGGAATCAGAGGCACTGT

MUC1R #6

MC1R #13

Tyros #16

K L T G D B N P T I P Y N D N R D A E K C D I C T D E Y N G

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AAGCTCACCGGAGACGAAAACTTTACCATTCCCTATTGGGATTGGAGAGACGCTGAGAAATGCGATATCTGTACCGATGAGTATATGGGA

gp100 #32

L R L V K R Q V P L D C V L Y R Y G S F S V T L D I V Q G I CTGAGACTGGTCAAGACACGCCTCGACATTGTGCAAGGCATT

MUCIR #10

PLQIYKQGGPLGLSNIKFRPGSVVVQLTLA

MC1R #9

V I D V I T C S S M L S S L C P L G A I A V D R Y I S I F Y GTGATTGACGTCATCACATGCTCCAGCATGCTCTCCAGCCTTTCTGGGAGCCATTGCCGTCGACAGATACATTAGCATTTTCTAT

Tyros #21

R N P G N H D K S R T P R L P S S A D V E P C L S L T Q Y E AGGAATCCCGGAAACCATGACAAAAGCAGAACCCCTAGGCTCCCCTCCAGCGCTGACGTCGAGTTTTGCCTCAGCCTCAGCCTCAATACGAA

TRP-1 #14

gp100 #39

V S L A D T N S L A V V S T Q L I M P G Q E A G L G Q V P L GTGTCCCTGGCTGACACAAACTCCCTGGCTGTGGTCAGCACACACTCATCATGCCCGGACAGGAAGCCGGACTGGGACAGGTCCCCCTC

gp100 #20

GPVTAQVVLQAAIPLTSCGSSPVPGTTDGH GGCCCTGTGACAGCCCAAGTGGTCCTGCAAGCCGTTGCCTTGCCAGCCCTTGCCAGCCCAACCGATGGCCAT

Tyros #8

K F G F W G P N C T E R R L L V R R N I F D L S A P E K D K AAGTITGGCTTTTGGGGACCCAATTGCACAGAGAGAGCTCCTGGTCAGGAGAACATTTTCGATCTGTCCGCCCCTGAGAAAGACAAA

gp100 #13

L G T H T M E V T V Y H R R G S R S Y V P L A H S S S A P T CTGGGAACCCATACCATGGGGGTCTACCTCCAGCGCTTTCACACACCCCTTCGCCCCATAGCTCCAGCGCTTTCACA

MC1R #12

TRP2 #25

G T L D S Q V M S L H N L V H S F L N G T N A L P H S A N GGCACACTGGATGGCCAGATGGCCTCCCCCATAGGGCTGCCAAT

MART #4

G C W Y C R R R R G Y R A L M D K S L H V G T Q C A L T R R GGCTGTTGGTATTGCAGAGGAGAACGGATACAGAGCCCTCATGGATAAGTCCCTGCATGTGGGAACCCAATGCGCTCTGACAAGGAGA

Tyros #15

PWHRLFLLRWEQEIQKLTGDENFTIPYWDWCCCTGGCACAGACTGTTCTCCTCAGGTGGGAGCAAACTGACAGCCGATGAGAATTTCACAATCCCTTACTGGGACTGG

MC1R #1

A A M A V Q G S Q R R L L G S L N S T P T A I P Q L G L A A GCCGCTATGGCTGCAGGGCTCCCAGGAGGCTCCCCGCTTCCCCCCTACCGCTATCCCTCAGCTCGCCTCCCCGCT

MCIR #5

V V A T I A K N R N L H S P N Y C P I C C L A L S D L L V S GTGGTCGCCACAATCGCTAAGAATAGGAATCTGCATAGCCCTATGTATTGCTTTATCTGTTGCCTCGCCCTCAGCGATCTGCTCGTGTCC

Tyros #25

Q S S M H N A L H I Y M N G T M S Q V Q G S A N D P I P L L CAGTCCAGCATGCACCATGCCCTCCACATTACATGAACGGAACCATGAGCCAAGTGCAAGGCTCCGCCAATGACCCTATCTTTCTGCTC

Tyros #18

G Q H P T N P N L L S P A S P F S S W Q I V C S R L B E Y N GGCCAACACCCTACCAATCCCAATCCCCAGCCTCCCTCCTTCTTTAGCTCCTGGCAAATCGTCTGCTCCAGGCTCGAGGAATACAAT

MCIR #6

Y C F I C C L A L S D L L V S G T N V L E T A V I L L E A

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TACTGTTTCATTTGCTGTCTGGCTCTGTCCGACCTCCTGGTCAGCCGAACCAATGTGCTCGAGACAGCCGTCATCCTCCTGCTCGAGGCT

TRP2 #19

MUCLF #8

T R P A L G S T T P P A H D V T S A P D N K A A ACCAGACCCGCTCGGGAAGCACCCCTCCCGCTCACGATGTGACAAGCGCTCCCGATAACAAGCCGCT

Tyros #17

R D A E K C D I C T D E Y M G G Q H P T N P N L L S P A S F AGGGATGCCGAAAAGTGTGCACAGACGAATACATGGGCGGACAGCATCCCACAAACCCTAACCTCCTGTCCCCCGCTAGCTTT

gp100 #17

T P A L Q L H D P S G Y L A B A D L S Y T W D P G D S S G T ACCTITECCCTCCACCTCCACCTCCCGCATCCCCCCCCCCACCACCTCACCTCACCTCCACCTCACACCTCACCTCACCTCACCTCACCTCACCTCACCTCACACCTCACCTCACCTCACCTCACACACACCTCACACTCACACACACACACACACACACCTCACACACACACACACACACACACACACACACAC

Tyros #22

SSADVEFCLSLTQYESGSMDKAANFSFRNT AGCTCCGCCGATGTGGAATTCTGTCTGTCCCTGACACACTATGAGTCCGGCTCCATGGATAAGGCTGCCAATTTCTCCTTCAGAAACACA

qp100 #6

MC1R #18

W G P F P L H L T L I V L C P E H P T C G C I F K N F N L F TGGGGACCCTTTTTCCTCCACCTCACCCTCATCGTGTCCCGGACACCCCTACCTGTGGCTGTATCTTTAAGAATTTCAATCTGTTT

Tyros #7

CQCSGNFMGFNCGNCKFGFWGPNCTERRLLTGCCAATGCTCCGGCCCTAACTGTACCGAAAGGAGACTGCTC

TRP2 #34

Q Y R R L R R G Y T P L M E T H L S S K R Y T E E A A A CAGTATAGGAGACTGAGAAAGGGATACACCCCTCATGGAAACCCATCTGTCCAGCAAAAGGTATACCGAAGAGGCTGCCGCT

TRP-1 #15

PLENAPIGHNRQYNMVPFWPPVTNTEMFVT

gp100 #7

N P P G S Q K V L P D G Q V I W V N N T I I N G S Q V W G G AACTITCCCGGAAGCCAAAGGTCCTGACGGACAGGTCATCTGGGTGAATAACACAATCATTAACGGAAGCCAAGTGTGGGGCGGA

gp100 #22

R P T A B A P N T T A G Q V P T T B V V G T T P G Q A P T A
AGGCCTACCGCTGAGGCTCCCAATACCACAGCCGGCACAGCCCCTACCGCT

MUCIF #3

S T P G G E K B T S A T Q R S S V P S S T E K N A V S M T S AGCACACCGGAGGGGGAAAAGGAAACCTCCGCCACAGAGAAGCTCCGTCGCCTAGCTCCACCGAAAAAGAATGCCGTCAGCATCACCTCC

gp100 #42

LIYRRRLMKQDPSVPQLPHSSSHWLRLPRI CTGATTTACAGAAGGAGACTGATGAAGCAAGACTTTAGCGTCCCCAACTGCCTCAGCTCCCACTGCCTCAGACTGCCTAGGATT

TRP2 #12

LGLLGPNGTQPQPANCSVYDPPVWLHYYSV
CTGGGACTGCTCGGCACCCAACCCCAATTCGCTAACTGTAGCGTCTACGATTTCTTTGTGTGGCTGCATTACTATAGCGTC

TRP-1 #9

C L E V G L P D T P P F Y S N S T N S F R N T V B G Y S D P
TGCCTCGAGGTCGGCCTCTTCGATACCCCTCCTTTTACTCCAACTCCACCAATAGCTTTAGGAATACCGTCGAGGGATACTCCGACCCT

gp100 #1

A A M D L V L K R C L L H L A V I G A L L A V G A T K V P R GCCGCTATGGATCTGGTCTGGAAAGGTGTCTCCACCTCACCTCATCGGAGCCCTCCTGGCTGTGGGAGCCACAAAGGTCCCCAGA

MC1R #3

NQTGARCLEVSISDGLPLSLGLVSLVENAL

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AACCAAACCGGAGCCAGATGCCTCGAGGTCAGCATTAGCGATGGCCTCTTCCTCAGCCTCGGCCTCGTGTCCCTGGAGAATGCCCTC

S G S M D K A A N F S P R N T L B G F A S P L T G I A D A S 

S P C G Q L S G R G S C Q N I L L S N A P L G P Q P P F T G AGCCCTTGCGGACAGCTCAGCGGAAGGGGAAGCTGTCAGAATATCCTCCTGTCCAACGCTCCCCTCGGCCCTCAGTTTCCCTTTACCGGA

Tyros #13

M H Y Y V S M D A L L G G S E I W R D I D F A H E A P A F L ATGCATTACTATGTGTCCATGGATGCCCTCCTGGGAGGGCTCCGAGATTTGGAGAGACATTGACTTTGCCCATGAGGCTCCCGCTTTCCTC

BEKQPLL MEKEDYHSLYQSHLAA GAGGAAAAGCAACCCCTCCTGATGGAGAAAGAGGATTACCATAGCCTCTACCAAAGCCATCTGGCTGCC

G Q C T E V R A D T R P W S G P Y I L R N Q D D R E L W P R GGCCANTGCACAGAGGTCAGGGCTGACACAAGGCCTTGGTCCGGCCCTTACATTCTGAGAAACCAAGACGATAGGGAACTGTGGCCCAGA

S V P S S T E K N A V S M T S S V L S S H S P G S G S S T T AGCGTCCCTCCAGCACAGAGAAAAACGCTGTGTCCATGACAAGCTCCGTGCTCAGCTCCCACTCCCCCGGAAGCGGAAGCTCCACCACA

TPMFNDINIYDLFVWMHYYVSMDALLGGSE 

gp100 #9

Q P V Y P Q B T D D'A C I F P D G G P C P S G S W S Q K R S CAGCCTGTGTATCCCCAAGAGACAGACGATGCCTGTATCTTTCCCGATGGCGGACCCTGTCCCTCGGCTCCTGGTCCCAGAAAAGGTCC

D S L E D Y D T L G T L C N S T E D G P I R R N P A G N V A GACTCCCTGGAAGACTATGACACACTGGGAACCCTCTGCAATAGCACAGAGGATGGCCCTATCAGAAGGAATCCCGCTGGCAATGTGGCT

gp100 #8

W V N N T I I N G S Q V W G G Q P V Y P Q E T D D A C I P P TGGTCAACAATACCATTATCAATGGCTCCCAGGTCTGGGGGGGCCAACCCGTCTACCCTCAGGAAACCGATGACGCTTGCATTTTCCCT

Q E K N C E P V V P N A P P A Y E K L S A E Q S P P P Y S P 

gp100 #14 SRSYVPLAHSSSAPTITDQVPPSVSVSQLR AGCAGAAGCTATGTGCCTCTGGCTCACTCCAGCTCCGCCTTTACCATTACCGATCAGGTCCCCTTTAGCGTCAGCGTCAGCCAACTGAGA

LEKDMQEMLQEPSPSLPYWNPATGKNVCDI 

V P F W P P V T N T E M P V T A P D N L G Y T Y E A A GTGCCTTTCTGGCCCCCTGTGACAACACAGAGATGTTCGTCACCGCTCCCGATAACCTCGGCTATACCTATGAGGCTGCC

TRP2 #13

C S V Y D P F V W L H Y Y S V R D T L L G P G R P Y R A I D TGCTCCGTGTATGACTTTTTCGTCTGGCTCCACTATTACTCCGTGAGAGACACACTGCTCGGCCCTGGCAGACCCTATAGGGCTATCGAT

V R R N I F D L S A P B K D K P F A Y L T L A K H T I S S D 

K K G H G H S Y T T A B E A A G I G I L T V I L G V L L L I AAGAAAGGCCATGGCCATAGCTATACCACAGCCGAAGAGGCTGCCGGAATCGGAATCCTCACCGTCATCCTCGGCGTCCTGCTCCTGATT

gp100 #11

PVYVWKTWGQYWQVLGGPVSGLSIGTGRAM

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TTCGTCTACGTCTCGGAAAACCTGGGGCCCAATACTGGCAGGTCCTGGGAGGCCCTGTGTCCGGCCTCAGCATTGGCACAGGCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCAGGCCAGGCCAGGCCAGGCCAGGCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCAGGCCA

gp100 #12

gp100 #25

Tyros #19

F S S W Q I V C S R L B B Y N S H Q S L C N G T P E G P L R TICTCCAGCTGGCAGATTGTGTGGCAGACTGGAAGAGTATAACTCCCACCAAAGCCTTGCAATGGCACACCCGAAGGCCCTCTGGAA

TRP2 #2

DPIPVVLHSFTDAIPDEWMKRPNPPADAWPGACCCTATCTTTGTGGTCCTGCCTGACGCTTGGCCTTTCGATGAGTGAAAAGGTTTAACCCTCCCGCTGACGCTTGGCCT

MC10 #15

H M L A R A C Q H A Q G I A R L H K R Q R P V H Q G F G L K CACATGCTGGCTAGGGCTTCCCACACACGCTCAGGGATTCGCTAGGCTCCACAAAGGCCAAAAGGCCTGTGCATCAGGGATTCGGACTGAAA

MUCLP #2

L L T V L T V V T G S G H A S S T P G G E K B T S A T Q R S CTGCTCACCGTCCTGACAGTCACCGTCACCGTACCCTACCCTACCCTACCCTCGCGGAGAGAAAAGAGACAAGCGCTACCCAAAGGTCC

qp100 #44

PCSCPIGBNSPLLSGQQVAA
TTCTGTAGCTGTCCCATTGGGGAAAACTCCCCCTCCTGTCCGGCCAACAGGTCGCCGCT

TRP2 #24

T P S P R N A L E G P D K A D G T L D S Q V M S L H N L V H
ACCITIAGCATTAGGAATGCCCCGAGGGATTCGATAACCTCGATGACGCATCCCAGGTCATGTCCCTGCATAACCTCGTGCAT

Tyros #20

TRP2 #30

PPPPVTNEBLPLTSDQLGYSYAIDLPVSVCCCTTTTTCCCTCCCGTCACCATGACGACTCTTTCTGACAAGCGATCAGCTCTGCCTATGCCTATGCCATTGACCTCCCGTCAGCGTC

TRP2 #

TRP2 #29

cm100 #28

EVSIVVLSGTTAAQVTTTEWVETTARELPI

MUCIR #7

T S P Q L S T G V S P P P L S P H I S N L Q P N S S L B D P ACCTCCCCCAACTGCCACTGCCAGTGCTCCTTCTTTTTCCTCAGCTTTCACATTGCCACTGCCAATTCAATAGCTCCCTGGAAGACCCT

MUC1R #19

YHTHGRYVPPSSTDRSPYEKVSAGNGGSSL
TACCATACCCATGCCAGATACGTCCCCCTAGCAGAGTCTCCGCCGGAAACGAGGCTCCACCCTC

MC1R #4

LPLSLGLVSLVENALVVATIAKNRNLHSPM CTGTTTCTGTCCCTGGGACTGGCAAAACGCTCTGGTCGTCGTCGCTACCATTGCCAAAAACAGAAACCTCCACTCCCCCATG

TRP2 #26

MUC1R #17

AVCQCRRENYGQLDIPPARDTYHPMSEYPT

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GCCGTCTGCCAATGCAGAAGGAAAAACTATGGCCAACTGGATATCTTTCCCGCTAGGGATACCTATCACCCTATGTCCGAGTATCCCACA

MC1R #14

V P P L A M L V L M A V L Y V H M L A R A C Q H A Q G I A R GTGTTTTTCCTCGCCATGCTCTGATGGCCGTCCTGTATGGCCATGCCCAGGCCTTCTCAGCATGCCCAAGGCATTGCCAGA

TRP-1 #10

S T N S F R N T V E G Y S D P T G K Y D P A V R S L H N L A AGCACAAACTCCTTCAGAAACACAGTGGAAGGCTTATAGGGTTCCCACAGGCAAATACGATCCCGCTGTGAGAAGCCTCCACAATCTGGCT

TRP-1 #3

L P Y W N F A T G K N V C D I C T D D L M G S R S N F D S T CTGCCTTACTGGAACTTTGCCACAGGCAAAAACGTCTGCGATATCTGTACCGATGACCTCATGGGAAGCAGAAGCAATTTCGATAGCACA

cm100 #19

MUC1R #8

MUCIR #20

S P Y E K V S A G N G G S S L S Y T N P A V A A A S A N L A AGCCCTTACGAAAAGGTCAGCGCTGGCAATGGCGGAAGCTCCCTGTCCTACACAAACCCTGCCGTCGCCGCTGCCTCCCCCAATCTGGCT

Tyros #11

Y V I P I G T Y G Q M K N G S T P M F N D I N I Y D L F V W TACGTCATCCCTATCGGAACCTAATGACAATGAAAAACCGGAAGCACCCCATGTTCAATGACATTAACATTTACGATCTGTTTGTGTGG

gp100 #37

m100 #33

RYGSPSVTLDIVQGIESAEILQAVPSGEGDAGGTATGGCTCCCTCCGGCGAAGGCGAT

Tyros #27

H H A F V D S I P E Q W L Q R H R P L Q E V Y P E A N A P I CACCATGCCTTTGGATAGCATTTTCGAACAGTGGCTGCAAAGGCCTAGGCCTCCAATT

TRP-1 #4

CTDDLMGSRSNPDSTLISPNSVPSQWRVVC

MUCIR #18

PPARDTYHPMSEYPTYHTHGRYVPPSSTDR

MIICIR #21

S Y T N P A V A A A S A N L A A AGCTATACCAATCCCGCTGGCTGCCGCTAGCGCTAACCTCGCCGCT

MC1R #19

Tyros #26

M S Q V Q G S A N D P I F L L H H A F V D S I F E Q W L Q R ATGTCCCAGGGCCCAGGGGAAGCGCTACGATCCCATTTTCCTCCTGCATCACGCTTTCGTCGACTCCATCTTTGAGCAATGGCTCCAGAGA

TRP2 #22

R N S M K L P T L K D I R D C L S L Q K P D N P P F P Q N S AGGAATAGCATGAAGCTCCCCACACTGAAAGACTTCCCACACACTCCCCTCTTTTCCAAAACTCC

gp100 #19

L I S R A L V V T H T Y L E P G P V T A Q V V L Q A A I P L CTGATTAGCAGAGCCCTCGTGGTCACCCATACCTATCTGGAACCCGGCCCGTCACCGCTCAGGTCGTGCTCCCAGGCTGCCATTCCCCTC

TRP2 #17

S P A L P Y W N P A T G R N B C D V C T D Q L F G A A R P D

### 176/216

gp100 #2

VIGALLAVGATKVPRNQDNLGVSRQLRTKA GTGATTGGCGCTCTGCCGCTCTGCCCTACCAAAGTGCCTAGGAATCAGGATTGGCTCGGCGTCAGCAGACAGCTCAGGACAAGGCT

ap100 #16

TRP2 #18

C D V C T D Q L F G A A R P D D P T L I S R N S R F S S W E TGCGATGTGTGTCCGATCACTCTTCGGAGCCCTGGCGACGATCCCACTGATTAGCAGAAACTCCAGGTTTAGCTCCTGGGAA

MART #

A A M P R E D A H P I Y G Y P K K G H G H S Y T T A E E A A GCCGCTATGCCTAGGGAAGACGCTCACTTTATCTATGGCTATCCCAAAAAGGGACACGGACACTCCTACAAACCGCTGAGGAAGCCGCT

TRP-1 #11

MIC1R #14

S D V S V S D V P F P P S A Q S G A G V P G W G I A L L V L AGCGATGTGTCCGGATGCGGCGTCCCCTTTCCCTTTAGCGCTCAGTCCGGCGTCCCCGGATGGGGATCGCTCTGTTCGTGCTC

TRP2 #10

S P Q B R B Q F L G A L D L A K K R V H P D Y V I T T Q H W AGCCCTCAGGAAAAGGGAACGGTTTCTGGGAGCCCTCGACCTGGCCAAAAAGGAGTGCATCCCGATTACGTCATCACAACCCAACACTGG

Tyros #10

PPAYLTLAKHTISSDYVIPIGTYGQACATACGACAGATGAGATGAGCTCC

MC1R #7

G T N V L E T A V I L L E A G A L V A R A A V L Q Q L D N GGCACAACGTCCTGGAACCGCTCTTGGATTCTGCTCCTGGAAGCCCGACGCCCTCCTGGCTAGGGCTGCCGTCCTGCACAGCTCGACAAT

MUC1R #16

V C V L V A L A I V Y L I A L A V C Q C R R K N Y G Q L D I GTGTGTGTGTGTGTGTGTGTGTGTGGGGGAAAGAATTACGGACAGCTCGACATT

MART #6

C P Q B G P D H R D S K V S L Q B K N C B P V V P N A P P A TGCCCTCAGGAAGGCTTTGACCATAGGGATAGCAAAGTGTCCCTGCAAGAGAAAAACTGTGAGCCTGTGGTCCCCAATGCCCCTCCCGCT

MUC1F #5

TRP2 #28

DEWMKRPNPPADAWPQBLAPIGHNRMYNMVGACGAATGGATGAATGGATGCATGCCCCCAAGAGCTCCCCCCTATCGGACACAATAGGATGTACAATATGGTC

MC1R #21

A P H S Q E L R R T L K E V L T C S W A A GCCTTTCACTCCCAGGAACTGAGAAGGACACTGAAAGAGGTCCTGACATGCTCCTGGGCTGCC

TRP2 #15

FSHQGPAFVTWHRYHLLCLERDLQRLIGNE
TTCTCCCACCAAGGCCCTGCCTTTGTGACATGGCATAGGTATCACCTCCTGTGTCTGGAAAGGGATCTGCAAAGGCTCATCGGAAACGAA

TRP-1 #8

R P M V Q R L P B P Q D V A Q C L B V G L F D T P P F Y S N AGGCCTATGGTCCAGAGACTGCCTGAGCCCTCAGGATGTGGCTCAGTGTCTGGAAGTGGGACTGTTTGACACCCCCTTTCTATAGCAAT

TRP-1 #13

Q D P I F V L L H T F T D A V F D E W L R R Y N A D I S T F CAGGATCCCATTTTCGTCCTCCTCACACACTTCACAGACGCTGTGTTTGACGAATGGCTCAGGAGATACAATGCCGATATCTCCACCTTT

TRP2 #4

LGAESANVCGSQQGRGQCTEVRADTRPNSG

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CTGGGAGCCGAAGCGCTAACGTCTGCGGAAGCCAACAGGGAAGGGGACAGTGTACCGAAGTGAGAGCCGATACCAGACCCTGGAGCGGA

TRP2 #8

YNCGDCKFGNTGPNCERKKPPVIRQNIHSL
TACAATTGCGGGGACTGTAAGTTTGGGTGGCCCGACTGGACAGAATATCCATAGCCTC

TRP-1 #12

H L P L N G T G G Q T H L S S Q D P I P V L L H T P T D A V CACCTCTTCCTCAACGGAACCGAACCCAACCCATCTGTCCAGGCCAAGACCCTATCTTTGTGCTCCTGCATACCTTTACCGATGCCGTC

Tyros #34

TRP2 #2

G C K I L P G A Q G Q P P R V C M T V D S L V N K B C C P R GGCTGTAAGATTCTGCCTGGCGCTCAGGGACAGTTTCCCAGAGTGTGTATGACAGTGGATAGCCTCGTGAATAAGGAATGCTGTCCCAGA

gp100 #43

Q L P H S S S H N L R L P R I P C S C P I G E N S P L L S G CAGCTCCCCCATAGCTCCAGCCATTGCTCAGCCCAGAATCTTTTGCTCCTGCCCTATCGGAGAGAATAGCCCTCTGCTCAGCGGA

ap100 #10

D G G P C P S G S W S Q K R S F V Y V W K T W G Q Y W Q V L GACGGAGGCCCTTGCCCTAGCGGAGCTGGGGCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGACAGTATTGGCAAGTGCTC

gp100 #3

N Q D W L G V S R Q L R T K A W N R Q L Y P E W T E A Q R L AACCAAGACTGGCTGGACTGGACTGAGTGTCCAGGCAACTCAAGGCTCGAACGACAGCTCTACCCTGAGTGGACCGAAGCCCAAAGGCTC

Tyros #14

I W R D I D F A H E A P A F L P W H R L F L L R W E Q E I Q ATCTGGAGGGATATCGATTCGCTCACGAAGCCCCTGCCTTTCTGCCTTGGCATAGGCTCTTCCTCTGAGATGGGAACAGGAAATCCAA

MUC1F #1

A A M T P G T Q S P F P L L L L T V L T V V T G S G H A S GCCGCTATGACACCCGGAACCCAAAGCCCTTTCTTTCTGCTCCTGCTCCTGACAGTGCTCACCGTCGTGACAGGCTCCGGCCATGCCTCC

MART #5

D K S L H V G T Q C A L T R R C P Q B G F D H R D S K V S L GACAAAAGCCTCCACGTCGGCACACGTGTGCCCTCACCAGAAGGTGTCCCCAAGAGGGGATTCGATCACAGAGACTCCAAGGTCAGCCTC

MUC1R #2

Tyros #24

LEGFASPLTGIADASQSSMHNALHIYMNGTCTGGAAGGCTTGCCTCACCGGAATCGCTGACGCTAGCCAAAGCTCCATGCATAACGCTCTGCATATCTATATGAATCGCACA

TPP2 #14

Tyros #1

A A M L L A V L Y C L L W S F Q T S A G H F P R A C V S S K GCCGCTATGCTCCTGCCTGTCCTCCTGCTCCTCCAAACCTCCGCCGGACACTTTCCCAGAGCCTGTGTGTCCAGCAAA

gp100 #35

A F E L T V S C Q G G L P K E A C M E I S S P G C Q P P A Q GCCTTTGAGCTCACCGTCAGCGCTCACCCCCCAAAGAGGCTTGCATGGAGATTAGCTCCCCCGGATGCCAACCCCCTGCCCAA

Tyros #6

V D D R B S W P S V F Y N R T C Q C S G N P M G P N C G N C GTGGATGACAGAGGTCCTGGCCTAGCGTCTTCTATAACAGAACCTGTCAGTGTGAGGGAAACTTTATGGGATTCAATTGCGGAAACTGT

gp100 #34

ESAEILQAVPSGEGDAFELTVSCQGGLPKEGAGTCCCCCAAGCCCGACTCCCTAAGGAGAGCGAGACCCTTTCGACTGTCCTGCCAAGCCGGACTGCCTAAGGAA

TRP2 #20

T V C D S L D D Y N H L V T L C N G T Y E G L L R R N Q N G

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ACCGTCTGCGATAGCCTCGACGATTACAATCACCTCGTGACACTGTGTAACGGAACCTATGAGGGACTGCTCAGGAGAAACCAAATGGGA

Tyros #5

LLS NAPLG PQPPFTGVDDRESNPSVFYNRT

MART #8

Y E K L S A E Q S P P P Y S P A A TACGAAAGCTCAGCGCTGAGCAAAGCCCCCCTTACTCCCCGCTGCC

gp100 #41

IVGILLVLMAVVLASLIYRRRLMKQDFSVP

MART #:

G I G I L T V I L G V L L L I G C W Y C R R R N G Y R A L M GGCATTGGCATTCTGACAGTGATTCTGGCAGTGCTTCTGCTCATCGGATGCTGATGGGAGAAGGAATGGCTATAGGGCTCTGATG

Tyros #31

Y S Y L Q D S D P D S P Q D Y I K S Y L B Q A S R I W S W L TACTCCTACCTCCAGGATAGCGATCCCGAGGATTCCTCCAGGATTTCGGCTCCTCCAGGATTTCGTCCTGGCTC

MUC1F #

Q G Q D V T L A P A T B P A S G S A A T W G Q D V T S V P V CAGGGACAGGATGTGACATGGCTCCCGCTACCGGAACCCGCTACCGGAACCCGCTACCGGAACCCGCTACCGGAACCCGCTACCGGAACCCGCTACCGGAACCCGCTACCGGAACCCGCTACCGGAACCCGCTACCGGAACCCGCTACCAGGATGTGACAAGCCTTCCCCGTC

ap100 #21

TSCGSSPVPGTTDGHRPTABAPNTTAGQVPACCTCCTGCGGAAGCTCCCCGGAACCACAGACGACCACAGACCGCAAGCCCCTAACAACCGCTGGCCAAGTGCCT

MUC1R #3

TRP2 #32

E E T P G W P T T L L V V M G T L V A L V G L P V L L A P L GAGGAAACCCTGGCTGGCCCACAACCCTCTGGTCGTCGTCGTCGTCGCCACACCTCTCGCCTTTCCTC

gp100 #29

T T T E N V B T T A R B L P I P E P B G P D A S S I M S T B ACCACAACCGAATGGGTCGAGACCAACCGAATGGGTCGAGAACCGCATGACGCATGACGGAACCGAA

MC1R #17

G A V T L T I L L G I P P L C W G P P P L H L T L I V L C P GGGGGTGGACACTGACACTCCTGCGGAATCTTTTTCCTCTGCGGGCCCTTTCTTCTGCACACTGACACTGATTGTGCTCTGCCCT

Tyros #33

L G A A M V G A V L T A L L A G L V S L L C R H K R K Q L P CTGGGAGCCGCTATGGTCGGCGCTGTCCACCGCCTCGCCGGACTGGTCAGCCATCAGGCATAAGAGAAAGCAACTGCCT

MC1R #8

G A L V A R A A V L Q Q L D N V I D V I T C S S M L S S L C GGGGCTCTGGTCGCCAGGCCGCTGTCCCCAGGCACTGGATAACGTCATCGATGTACCTCATGCTCAGCTCCATGCTCAGCTCCCTGTGT

cm100 #26

M T P E K V P V S E V M G T T L A E M S T P E A T G M T P A
ATGACACCCGAAAAGGTCCCCGTCAGCGAAGTGACACCCCCCTCGCCGAAATGTCCACCCCTGAGGCTACCGGAATGACACCCCCCT

Tyros #2

MC1R #11

A L R Y H S I V T L P R A P R A V A A I W V A S V V F S T L GCCCTCAGGTATCACTCCATCGTCACCCCCCAGAGCCCCTAGGGCTGTGCCATTTGGGTCGCCTCCGTGGTCTTCTCCACCCTC

MUC1R #12

FREGTINVHDVETQFNQYKTEAASRYNLTI TTCAGAGAGGGAACCATTAACGTCCACGATGTGGAAACCCAATTCAATCAGTATAAGACAGAGGCTGCCTCCAGGTATAACCTCACCATT

Tyros #3

N L M B K B C C P P W S G D R S P C G Q L S G R G S C Q N I

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AACCTCATGGAAAAGGAATGCTGTCCCCCTTGGTCCGGCGATAGGTCCCCCTGTGGCCAACTGTCCGGCAGAGGCTCCTGCCAAAACATT

Tyros #32

I K S Y L E Q A S R I W S W L L G A A M V G A V L T A L L A ATCAAAAGCTATCTGGAACAGCTAGCAGAATCTGGAGCTGCTGGCGCTGCCATGGTGGAGCCGTCCTGACAGCCCTCCTGGCT

MUCLR #5

MUC1R #15

S G A G V P G W G I A L L V L V C V L V A L A I V Y L I A L AGGGGAGGCCGGAGTGCCTGGCCATTGCCTCCTGGTCCTGGTCCTGGTCCTGGTCCTGGTCCTGGCCATTGTTATCTGATTGCCCTC

MC1R #10

F L G A I A V D R Y I S I F Y A L R Y H S I V T L P R A P R TTCCTCGGGGCTATCGCTGTGGATAGGTATATCTCCATCTTTTACGCTCTGAGATACCATAGCATTGTGACACTGCCTAGGGCTCCCAGA

gp100 #40

L I M P G Q B A G L G Q V P L I V G I L L V L M A V V L A S CTGATTATGCCTGCCCAGAGGCCTGCCCAAGTGCCTCTGATTGTGGGAATCCTCCTGGTCCTGATGGCCGTCGTGCTCGCCCTCC

TRP2 #33

T L V A L V G L F V L L A F L Q Y R R L R K G Y T P L M E T ACCUTCGIGGCTCTGGTCGGCCTCTTCGTCTCGCCTTTCTGCATACAGAAGGCTCAGGAAAGGCTATACCCCTCTGATGGAGACA

TRP-1 #5

L I S P N S V F S Q W R V V C D S L E D Y D T L G T L C N S CTGATTAGCCCTAACTCCGTGTTTAGCCAATGGAGGGTGGTCTGCGATAGCCTCGAGGATTACCGTGTAACTCC

MC1R #2

L N S T P T A I P Q L G L A A N Q T G A R C L E V S I S D G CTGAATAGCACACCCACAGCCATTCCCCAACTGGGACTGCCTAATCAGACAGGCGCTAGGTGTCTGGAAGTGTCCATCTCCGACGGA

Tyros #28

HRPLQEVYPEANAPIGHNRESYMVPFIPLY

gp100 #24

EPSGTTSVQVPTTEVISTAP.VQMPTAESTGGAGCCTAGCGGAACCAAGCGTCCAGGTCCCCCACAACCGAAGTGATTAGCACAGCCCCTGTGCAAATGCCTACCGCTGAGTCCACCGGA

TRP2 #11

KKRVHPDYVITTQHWLGLLGPNGTQPQFAN AAGAAAAGGGTCCACCCTGACTATGTGATTACCACAGCATTGGCTCGGCCTCCTGGGACCCAATGGCACACGCCTCAGTTTGCCAAT

gp100 #38

LHQILKGGSGTYCLNVSLADTNSLAVVSTQ CTGCATCAGATTCTGAAAGGCGGAAGCGGAACCTATTGCCTCAACGTCAGCCTCGCCGATACCAATAGCCTCGCCGTCGTGTCCACCCAA

m100 #30

cm100 #31

SITGSLGPLLDGTATLRLVKRQVPLDCVLY
AGCATTACCGGAAGCCTCCGGCCCCCCCCGAACCGCCTCCCCCCGAAAAGGCAAGCCCACCCCCCGATGAAAAGGCAAGTGCCTCCGGATGCCTCCTGTAT

gp100 #5

D C W R G G Q V S L K V S N D G P T L I G A N A S P S I A L GACTGTTGGAGAGGCGGACAGGTCAGGCTCAAGGTCAGGCATGACGCACCCACACTGATTGGCGCTAACGCTAGCTTTAGCATTGCCCTC

Synthetic Protein:

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WHRQLYPEWTEAGRLDCWRGGQVSLKVSNDPYILRNQDDRELMPRKPPHRTCKCTGNPAGRNGDPFISSKDLGYDYSYLQDSDPDSPQDYAAPAFLTW
HRYHLLRLBKDWQEWLQBPSFYSGHRESYMVPPIPLYRNGDFPISSKDLGYDLLCLERDLQRLIGNESFALPYWNFATGRNETTEVVGTTPGQAPTAE
PSGTTSVQVPTTEVSTDYYQELQRDISEMFLQIYKQGGFIGLSWACMEISSFGCQPPAQRLCQPVLPSPACQLVDQLGYSYAIDLPVSVEBTPGMPTT
LLVVMGTEDGPIRRNPAGNVARFMVQRLPBPQDVAQCMTVDSLVMKECCFRLGAESANVCGSQQGRNQYKTEAASRYMLTISDVSVSDVPPPPSAQAA
MSPLMWGFLLSCLGCKILPGAQGQPPRVADLSYTWDFGDSSGTLISRALVVTHTYLBPLAEMSTPEATGMTPAEVSIVVLSGTTAAQVIKPRPGSVVV
QLTLAFREGTINVHDVBTQFGSAATMGQDVTSVPVTRPALGSTTPPAHDVLHKRQRPVHQGFGLKGAVTLTILLGIPPLCLALIICNAIIDPLIYAPH
SQELRRTLKEVLKFFHRTCKCTGNFAGYNCGDCKFGWTGPNCLSLQKPDMPPFPQNSTPSFFRNALEGFDKADSKSTPPSIPSHHSDTPTTLASHSTKT
DASSAANRPALGSTAPPVHNVTSASGSASGSASTCMGTYEGLLRRNQMGRNSMKLPTLKDIRDCTHHSSVPPLISSHSTSPQLSTGVSFFFLSFIAY

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YDHVAVLLCLVVPPLAMLVLMAVLYVKLTGDENFTI PYWDWRDAEKCDICTDEYMGLRLVKRQVPLDCVLYRYGSPSVTLDIVQGIPLQIYKQGGPLG lsnikprpgsvvvqltlavidvitcssmlsslcflgaiavdryisifyrnpgnhdksrtprlpssadvefclsltqybfdewlrrynadistpplena pighnrqynmvsladtnslavvstqlimpgqeaglgqvplgpvtaqvvlqaaipltsccsspvpgttdghkpgfwgpncterrllvrrnipdlsapek dkigthtmevtvyhrrgsrsyvplahsssaptavaaiwvasvvpstlpiayydhvavllclvgtldsqvmslhnlvhsflngtnalphsaangcwycr rrngyralmdkslhvgtqcaltrrpwhrlpllrweqbiqkltgdenftipywdwaamavqgsqrrllgslnstptaipqlglaavvatiaknrnlhsp nycficclalsdllvsqssmhnalhiymngtmsqvqgsandpifllgqhptnpnllspasffsswqivcsrleeynycficclalsdllvsgtnvlbt hdpsgylaradlsytwdfgdssgtssadvefclsltqyesgsmdkaanpsfrntgptliganaspsialnppgsqkvlpdgqviwgppflhltlivlc PEHPTCGC1PKNFNLPCQCSGNFMGPNCGNCKFGPWGPNCTERRLLQYRRLRKGYTPLMETHLSSKRYTEEAAAPLENAP1GHNRQYNMVPFWPPVTN TEMFVTNFPGSQKVLPDGQVIWVNNTIINGSQVWGGRPTAEAPNTTAGQVPTTEVVGTTPGQAPTASTPGGEKBTSATQRSSVPSSTEKNAVSMTSLI YRRRLMKQDFSVPQLPHSSSHWLRLPRILGLLGPNGTQPQFANCSVYDFFVWLHYYSVCLEVGLFDTPPFYSNSTNSFRNTVEGYSDPAAMDLVLKRC llhlavigallavgatkvprnqtgarclevsisdglplsiglvslvenalsgsmdkaanfsfrntlegfaspltgiadasspcgqlsgrgscqnills naplgpqfpptcmhyyvsmdallggseiwrdidfaheapafleekqpllmekedyhslyqshlaagqctevradtrpwsgpyilrnqddrelwprsvp SSTEKNAVSMTSSVLSSHSPGSGSSTTTPMFNDINIYDLFVWMHYYVSMDALLGGSEQPVYPQETDDACIFPDGGPCPSGSWSQKRSDSLEDYDTLGT  $\textbf{LCNSTEDGPIRRNPAGNVAWVNNTIINGSQVWGGQPVYPQETDDACIFPQEKNCEPVVPNAPPAYEKLSAEQSPPPYSPSRSYVPLAHSSSAFTITDQ$ vppsvsvsqlrlekdmqemlqbpspslpymnpatgknvcdivppmppvtntempvtapdnlgytybaacsvydpppvwlhyysvrdtligpgrpyraid vrrnipdlsapekdxppayltlakhtissdkkghghsyttaeeaagigiltvilgvlllipvyvwkthgqywqvlggpvsglsigtgramggpvsgls igtgramlgthtmevivyhrrgistapvqmptaestgmtpekvpvsevmgttpsswqivcsrleeynshqslcngtpegplrdpipvvlhsftdaipd ewmkrfnppadawphmlaracqhaqgiarlhkrqrpvhqgfglklltvltvvtgsghasstpggeketsatqrspcscpigenspllsgqqvaatpsf rnalegpdkadgtldsqvmslhnlvhshqslcngtpegplrrnpgnhdksrtprlppppppvtneelpltsdqlgysyaidlpvsverkkppvirqni hslspqereqpigaldlaqbiapighnrmynmvpffppvineelpitsevsivvlsgttaaqvittewvettarelpitspqlstgvsffflsphisn LQPNSSLEDPYHTHGRYVPPSSTDRSPYEKVSAGNGGSSLLPLSLGLVSLVENALVVATIAKNRNLHSPMSFLNGTNALPHSAANDPIPVVLHSPTDA IPAVCQCRRKNYGQLDIPPARDTYHPMSEYPTVFFLAMLVLMAVLYVHMLARACQHAQGIARSTNSPRNTVEGYSDPTGKYDPAVRSLHNLALPYWNP atgknvcdictddlmgsrsnfdstitdqvppsvsvsqlraldggnkhflrnqplfhisnlqfnssledpstdyyqelqrdisemspyekvsagnggs LSYTNPAVAAASANLAYVIPIGTYGQMKNGSTPMFNDINIYDLFVWRLCQPVLPSPACQLVLHQILKGGSGTYCLNRYGSPSVTLDIVQGIESABILQ  ${\tt AVPSGESDHHAFVDSIPEQWLQRHRPLQEVYPEANAPICTDDLMGSRSNFDSTLISPNSVFSQWRVVCPPARDTYHPMSEYPTYHTHGRYVPPSSTDR$  ${\tt SYTNPAVAAASANLAAKHPTCGCIFKNFNLFLALIICNAIIDPLIYMSQVQGSANDPIFLLHHAFVDSIFEQWLQRRNSMKLPTLKDIRDCLSLQKFD$ NPPPPQNSLISRALVVTHTYLEPGPVTAQVVLQAAIPLSFALPYWNFATGRNECDVCTDQLFGAARPDVIGALLAVGATKVPRNQDWLGVSRQLRTKA ALDGGNKHPLRNQPLTFALQLHDPSGYLAECDVCTDQLPGAARPDDPTL1SRNSRFSSWEAAMPREDAHF1YGYPKKGHGHSYTTABEAATGKYDPAV rslinlahlpingtggqthlsssdvsvsdvppppsaqsgagvpgwg1allvlspqereqplgaldlakkrvhpdyv1ttqhwffayltlakht1ssdy VIPIGTYGQMKNGSGTNVLETAVILLLEAGALVARAAVLQQLDNVCVLVALAIVYLIALAVCQCRRKNYGQLDICPQBGPDHRDSKVSLQBKNCBPVV PNAPPASVLSSHSPGSGSSTTQGQDVTLAPATEPASDEWMKRFNPPADAWPQELAPIGHNRMYNMVAFHSQELRRTLKEVLTCSWAAFSHQGPAFVTW HRYHLLCLERDLQRLIGNERPMVQRLPEPQDVAQCLEVGLFDTPPFYSNQDPIPVLLHTFTDAVPDEWLRRYNADISTFLGAESANVCGSQQGRGQCT EVRADTRPWSGYNCGDCKFGWTGPNCERKKPPVIRQNIHSLHLFLNGTGGQTHLSSQDPIFVLLHTFTDAVGLVSLLCRHKRKQLPEEKQPLLMRKED yhsgckilpgaqgpprvcmtvdslvnkeccprqlphssshmlrlpripcscpigenspllsgdggpcpsgswsqkrspvyvmtwgqywqvlnqdwl GVSRQLRTKAWNRQLYPEWTEAQRLIWRDIDFAHEAPAPLPWHRLFLLRWEQBIQAAMTPGTQSPFFLLLLLTVLTVVTGSGHASDKSLHVGTOCALT rrcpqbgfdhrdskvslnvtsasgsasgsastlvhngtsaratttpalbgfaspltgiadasqssmhnalhiymngtrdtllgpgrpyraidfshqgp apvtwhryhaamllavlycilnspqtsaghppracvsskapeltvscqgglpkeacmbisspgcqppaqvddreswpsvfynrtcqcsgnfmgpncgn Cesabilqavpsgegdapeltvscqgglpketvcdslddynhlvtlcngtyegllrnqmgllsnaplgpqppptgvddreswpsvpynrtyeklsab QSPPPYSPAAIVGILLVIMAVVLASLIYRRRIMKQDFSVPGIGILTVILGVILLIGCWYCRRRNGYRALMYSYLQDSDPDSFQDYIKSYLEQASRIWS wlqqqdvtlapatepasgsaatmqqdvtsvpvtscqsspvpgttdghrptaeapnttagqvplvhngtsaratttpaskstppsipshhsdtretpgw PTTLLVVMGTLVALVGLPVLLAPLTTTEWVETTARELPI PEPEGPDASSIMSTEGAVTLTILLGI PFLCMGPFFLHLTLIVLCPLGAAMVGAVLTALL aglvsllcrhkrkqlpgalvaraavlqqldnvidvitcssmlsslcmtpekvpvsevmgttlaemstpeatgmtpaqtsaghppracvssknlmekec CPPWSGDRALRYHSIVTLPRAPRAVAAIWVASVVFSTLFREGTINVHDVETQFNQYKTEAASRYNLTINLMEKECCPPWSGDRSPCGQLSGRGSCONI iksyleqasriwswligaamvgavltallapttlashstktdassthhssvppltssnhssgagvpgwgiallvlvcvlvalaivylialplgaiavd RYISIFYALRYHSIVTLPRAPRLIMPGQEAGLGQVPLIVGILLVIMAVVLASTLVALVGLPVLLAPLQYRLRKGYTPLMETLISPNSVFSQWRVVCD  ${\tt SLEDYDTLGTLCNSLNSTPTAIPQLGLAANQTGARCLEVSISDGHRPLQEVYPEANAPIGHNRESYMVPPIPLYEPSGTTSVQVPTTEVISTAPVQMP$  ${\tt TABSTGKKRVHPDYVITTQHNLGLLGPNGTQPQFANLHQILKGGSGTYCLNVSLADTNSLAVVSTQPEPEGPDASSINSTESITGSLGPLLDGTATSI$ TGSLGPLLDGTATLRLVKRQVPLDCVLYDCWRGGQVSLKVSNDGPTLIGANASPSIAL

### Synthetic DNA:

TGGAATAGGCAACTGTATCCCGAATGGACAGAGGCTCAGAGACTGGATTGCTGGAGGGGGAGGCCAAGTGTCCCTGAAAGTGTCCCAACGATCCCTATAT TTATCTCCAGCAAAGACCTCGGCTATGACTATAGCTATCTGCAAGACTCCGACCCTGACTCCTTCCAAGACTATGCCGCTCCCGCTTTCCTCACCTGG CACAGATACCATCTGCTCAGGCTCGAGAAAGACATGCAGGAAATGCTCCAGGAACCCTCCTTCTCCGGCCCATAACAGAGAGTCCTACATGGTGCCTTT ATGAGTCCTTCGCTCTGCCTTACTGGAACTTTGCCACAGGCAGAAACGAAACCACAGGGTCGTGGGAACCACACCCGGACAGGCTCCCACAGCCGAA CCCTCCGGCACAACCTCCGTGCAAGTGCCTACCACAGAGGTCAGCACAGACTATTACCAAGAGCTCCAGAGAGACATTAGCGAAATGTTTCTGCAAAT CTATAAGCAAGGCGGATTCCTCGGCCTCAGCAATGCCTGTATGGAAATCTCCAGCCCTGGCTGTCAGCCTCCCGCTCAGAGACTGTGTCAGCCTGTGC TCCCCTCCCCGCTTGCCAACTGGTCGACCAACTGGGATACTCCTACGCTATCGATCTGCCTGTGTCCGTGGAAGAGACACCCGGATGGCCTACCACA CTGCTCGTGGTCATGGGAACCGAAGACGGACCCCATTAGGAGAACCCTGCCGGAAACGTCGCCAGACCCCATGGTGCAAAGGCTCCCCGAACCCCAAGA GAAACCAATACAAAACCGAAGCCGCTAGCAGATACAATCTGACAATCTCCGACGTCAGCGTCAGCGATGTGCCTTTCCCCTTTCTCCGCCCAAGCCGCT ATGTCCCCCCTCTGGTGGGGCTTTCTGCTCAGCTGTCTGGGATGCAAAATCCTCCCCGGAGCCCAAGGCCAATTCCCTAGGGTCGCCGATCTGTCCTA AAGCCACAGGCATGACCCCTGCCGAAGTGTCCATCGTCGTGCTCAGCGGAACCACAGCCGCTCAGGTCATCAAATTCAGACCCGGAAGCGTCGTGGTC GCCTGTGACAAGGCCTGCCCTCGGCTCCACCACCCCCTGCCCATGACGTCCTGCATAAGAGACAGAGACCCGTCCACCAAGGCTTTGGCCTCAAGG GAGCOGTCACCCTCACCATTCTGCTCGGCATTTTCTTTCTGTGTCTGGCTCTGATTATCTGTAACGCTATCATTGACCCTCTGATTTACGCTTTCCAT AGCCAAGAGCTCAGGAACCCTCAAGGAAGTGCTCAAGTTTTTCCATAGGACATGCAAATGCACAGGCAATTTCGCTGGCTATAACTGTGGCGATTG 

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GACGCTAGCTCCGCCGCTAACAGACCCGCTCTGGGAAGCACAGCCCCCTCCCGTCCACAATGTGACAAGCGCTAGCGGAAGCGCTAGCGGAAGCGCTAG CACATGCAATGCCACATACGAAGGCCTCCTGAGAAGGAATCAGATGGGCAGAAACTCCATGAAACTGCCTACCCTCAAGGATATCAGAGACTGTACCC TACGATCACGTCGCCGTCCTCGTCGTCGTCTTCTTTCTGGCTATGCTCGTGCTCATGGCTGTGCTCTACGTCAAGCTCACCGGAGACGAAAA CTTTACCATTCCCTATTGGGATTGGAGAGACGCTGAGAAATGCGATATCTGTACCGATGAGTATATGGGACTGAGACTGGTCAAGAGACAGGTCCCCC TCGACTGTGTGCTCTACAGATACGGAAGCTTTAGCGTCACCCTCGACATTGTGCAAGGCATTTTCCTCCAGATTTACAAACAGGGAGGCTTTCTGGGA CTGTCCAACATTAAGTTTAGGCCTGGCTCCGTGGTCGTGCAACTGACACTGGCTGATTGACGTCATCACATGCTCCAGCATGCTGCCAGCCTGTG CTITCTGGGAGCCATTGCCGTCGACAGATACATTAGCATTTTCTATAGGAATCCCGGAAACCATGACAAAAGCAGAACCCCTAGGCTCCCCTCCAGCG CTGACGTCGAGTTTTGCCTCAGCCTCACCCAATACGAATTCGATGAGTGGCTGAGAAGGTATAACGCTGACATTAGCACATTCCCTCTGGAAAACGCT  $\tt CGGACTGGGACAGGTCCCCCTCGGCCCTGTGACAGCCCAAGTGGTCCTGCAAGCCGCTATCCCTCTGACAAGCTGTGGCTCCAGCCCTGTGCCTGGCA$ GACAAACTGGGAACCCATACCATGGAGGTCACCGTCTACCATAGGAGAGGGCTCCAGGTCCTACGTCCCCCTCGCCCATAGCTCCAGCGCTTTCACAGC CGTCGCCGCTATCTGGGTGGCTAGCGTCGTGTTTAGCACACTGTTTATCGCTTACTATGACCATGTGGCTGGTCTGTGTCTGGTCGGCACACTGG AGGAGAAACGGATACAGAGCCCTCATGGATAAGTCCCTGCATGTGGGAACCCAATGCGCTCTGACAAGGAGACCCTGGCACAGACTGTTTCTGCTCAG GTGGGAGCAAGAGATTCAGAAACTGACAGGCGATGAGAATTTCACAATCCCTTACTGGGACTGGGCCGCTATGGCTGCCAAGGCTCCCAGAGAAGGC TCCTGGGAAGCCTCAACTCCACCCCTACCGCTATCCCTCAGCTCGGCCTCGCCGCTGTGGTCGCCACAATCGCTAAGAATAGGAATCTGCATAGCCCT ATGTATTGCTTTATCTGTTGCCTCGCCCTCAGCGATCTGCTCGTGTCCCAGTCCAGCATGCACAATGCCCTCCACATTTACATGAACGGAACCATGAG CCAAGTGCAAGGCTCCGCCAATGACCCTATCTTTCTGCTCGGCCAACACCCTACCAATCCCAATCTGCTCAGCCCTGCCTCCTTCTTTAGCTCCTGGC aaatcgtctgctccaggctcgaggaatacaattactgtttcatttgctgtctggctctgtccgacctcctggtcagcgaaccaatctgctcgagaca  ${\tt GCCGTCATCCTCGTGGAGGCTGACCCTACCCTCATCTCCAGGAATAGCAGATTCTCCAGGTGGGAGACAGTGTGTGACTCCCTGGATGACTATAA}$ CCATCTGGTCACCTCACCAGACCCGGCTCTGGGAAGCACAACCCCTCCCGCTCACGATGTGACAAGCGCTCCCGATAACAAAGCCGCTAGGGATGCCG AAAAGTGTGACATTTGCACAGACGAATACATGGGCGGACAGCATCCCACAAACCCTAACCTCCTGTCCCCCGCTAGCTTTACCTTTGCCCTCCAGCTC CACGATCCCTCCGGCTATCTGGCTGAGGCTGACCTCAGCTATACCTGGGACTTTGGCGATAGCTCCGGCACAAGCTCCGCCGATGTGGAATTCTGTCT GTCCCTGACACAGTATGAGTCCGGCTCCATGGATAAGGCTGCCAATTTCTCCTTCAGAAACACAGGCCCTACCCTCATCGGAGCCAATGCCTCCTTCT  ${\tt CCATCGCTCTGAATTTCCCTGGCTCCCGGAAAGTGCTCCCCGATGGCCAAGTGATTTGGGGGACCCTTTTTCCTCCACCTCACCCTCATCGTCCTGTGT\\$  $\tt CCCGAACACCCTACCTGTGGCTGTATCTTTAAGAATTTCAATCTGTTTTGCCAATGCTCCGGCAATTTCATGGGCTTTAACTGTGGCAATTGCAAATT$ CGGATTCTGGGGCCCTAACTGTACCGAAAGGAGACTGCTCCAGTATAGGAGACTGAGAAAGGGATACACACCCCTCATGGAAACCCATCTGTCCAGCA AAAGGTATACCGAAGAGGCTGCCGCTCCCCTCGAGAATGCCCCCTATCGGACACAATAGGCAATACAATATGGTCCCCTTTTGGCCTCCCGTCACCAAT GTGGGGCGGAAGGCCTACCGCTGAGGCTCCCAATACCACAGCCGGACAGGTCCCCACAACCGAAGTGGTCGGCACAACCCCTGGCCAAGCCCCTACCG CTAGCACACCCGGAGGCGAAAAGGAAACCTCCGCCACACAGAGAAGCTCCGTGCCTAGCTCCACCGAAAAGAATGCCGTCAGCATGACCTCCCTGATT TACAGAAGGAGACTGATGAAGCAAGACTTTAGCGTCCCCCAACTGCCTCACTCCAGCTCCCACTGGCTGAGACTGCCTAGGATTCTGGGACTGCTCGG CCCTAACGGAACCCAACCCCAATTCGCTAACTGTAGCGTCTACGATTTCTTTGTGTGGCTGCATTACTATAGCGTCTGCCTCGAGGTCGGCCTCTTCG ATACCCCTCCCTTTTACTCCAACTCCACCAATAGCTTTAGGAATACCGTCGAGGGATACTCCGACCCTGCCGCTATGGATCTGGTCCTGAAAAGGTGT CTGCTCCACCTCGCCGTCATCGGAGCCCTCCTGGCTGTGGGAGCCACAAAGGTCCCCAGAAACCAAACCGGAGCCAGATGCCTCGAGGTCAGCATTAG CGATGGCCTCTTCCTCAGCCTCGGCCTCGTGTCCCTGGTCGAGAATGCCCTCAGCGGAAGCATGGACAAAGCCGCTAACTTTAGCTTTAGGAATACCC TCGAGGGATTCGCTAGCCCTCTGACAGGCATTGCCGATGCCTCCAGCCCTTGCGGACAGCTCAGCGGAAGGGGGAAGCTGTCAGAATATCCTCCTGTCC AACGCTCCCCTCGGCCCTCAGTTTCCCTTTACCGGAATGCATTACTATGTGTCCATGGATGCCCTCCTGGGAGGCTCCGAGATTTGGAGAGACATTGA CTTTGCCCATGAGGCTCCCGCTTTCCTCGAGGAAAAGCAACCCCTCCTGATGGAGAAAGAGGATTACCATAGCCTCTACCAAAGCCATCTGGCTGCCG GCCAATGCACAGAGGTCAGGGCTGACACAAGGCCTTGGTCCGGCCCTTACATTCTGAGAAACCAAGACGATAGGGAACTGTGGCCCAGAAGCGTCCCC TCCAGCACAGAGAAAAACGCTGTGTCCATGACAAGCTCCGTGCTCAGCTCCCACCTCCCCGGAAGCGGGAAGCTCCACCACAACCCCTATGTTTAACGA TATCAATATCTATGACCTCTTCGTCTGGATGCACTATTACGTCAGCATGGACGCTCTGCTCGGCGGAAGCGGAACAGCCTGTGTATCCCCAAGAGACAG ACGATGCCTGTATCTTTCCCGATGGCGGACCCTGTCCCTCCGGCTCCTGGTCCCAGAAAAGGTCCGACTCCCTGGAAGACTATGACACACTGGGAACC CTCTGCAATAGCACAGAGGATGGCCCTATCAGAAGGAATCCCGCTGGCAATGTGGCTTGGGTCAACAATACCATTATCAATGGCTCCCAGGTCTGGGG AGGCCAACCCGTCTACCCTCAGGAAACCGATGACGCTTGCATTTTCCCTCAGGAAAAGAATTGCGAACCCGTCGTGCCTAACGCTCCCCCTGCCTATG AGAAACTGTCCGCCGAACAGTCCCCCCCCCCCCTATAGCCCTAGCAGAAGCTATGTGCCTCTGGCTCACTCCAGCTCCGCCTTTACCATTACCGATCAG GTCCCCTTTAGCGTCAGCCTCAGCCAACTGAGACTGGAAAAGGATATGCAAGAGATGCTGCAAGAGCCTAGCTTTAGCCTCCCCTATTGGAATTTCGC TACCGGAAAGAATGTGTGTGACATTGTGCCTTTCTGGCCCCCTGTGACAAACACAGAGATGTTCGTCACCGCTCCCGATAACCTCGGCTATACCTATG AGGCTGCTGCTCCGTGTATGACTTTTTCGTCTGGCTCCACTATTACTCCGTGAGAGACACACTGCTCGGCCCTGGCAGACCCTATAGGGCTATCGAT CCATGGCCATAGCTATACCACAGCCGAAGAGGCTGCCGGAATCGGAATCCTCACCGTCATCCTCGGCGTCCTGCTCCTGATTTTCGTCTACGTCTGGA AAACCTGGGGCCAATACTGGCAGGTCCTGGGAGGCCCTGTGTCCGGCCTCAGCATTGGCACAGGGCAGAGCCATGGGCGGACCCGTCAGCGGACTGTCC ATCGGAACCGGAAGGGCTATGCTCGGCACACACACAATGGAAGTGACAGTGTATCACAGAAGGGGGAATCTCCACCGCTCCCGTCCAGATGCCCACAGC ATAACTCCCACCAAAGCCTCTGCAATGGCACACCCGAAGGCCCTCTGAGAGACCCTATCTTTGTGGTCCTGCATAGCTTTACCGATGCCATTTTCGAT GAGTGGATGAAAAGGTTTAACCCTCCCGCTGACGCTTGGCCTCACATGCTGGCTAGGGCTTGCCAACACGCTCAGGGAATCGCTAGGCTCCACAAAAG GCAAAGGCCTGTGCATCAGGGATTCGGACTGAAACTGCTCACCGTCCTGACAGTGGTCACCGGAAGCGGACACGCTAGCTCCACCCCTGGCGGAGAGA AAGAGACAAGCGCTACCCAAAGGTCCTTCTGTAGCTGTCCCATTGGCGAAAACTCCCCCCTCCTGTCCGGCCAACAGGTCGCCGCTACCTTTAGCTTT AGGANTGCCCTCGAGGGATTCGATAAGGCTGACGGAACCCTCGACTCCCAGGTCATGTCCCTGCATAACCTCGTGCATAGCCATCAGTCCCTGTGTAA CACTCCCTGTCCCCCAAGAGAGAGAGAGCAATTCCTCGGCGCTCTCGGATCTGGCTCAGGAACTGGCTCCCATTGGCCATAACAGAATGTATAACATGGT GCCTTTCTTTCCCCCTGTGACAAACGAAGGCTCTTCCTCACCTCCGAGGTCAGCATTGTGGTCCTGTCCGGCACAACCGCTGCCCAAGTGACAACCA  ${\tt CAGAGTGGGTAGACCACAGGCGAGAGGGTCCCCCATTACCTCCCCCCAACTGTCCACCGGAGTGTCCTTCTTTTTCCTCAGCTTTCACATTAGCAAT}$ CTGCAATTCAATAGCTCCCTGGAAGACCCTTACCATACCCATGGCAGATACGTCCCCCTAGCTCCACCGATAGGTCCCCCTATGAGAAAGTGTCCGC CGGAAACGGAGGCTCCAGCCTCCTGTTTCTGTCCCTGGGACTGGTCAGCCTCGTGGAAAACGCTCTGGTCGTGGCTACCATTGCCAAAAACAGAAACC TCCACTCCCCATGAGCTTTCTGAATGGCACAAACGCTCTGCCTCACTCCGCCGCTAACGATCCCATTTTCGTCGTGCTCCACTCCTTCACAGACGCCT ATCTTTGCCGTCTGCCAATGCAGAAGGAAAAACTATGGCCAACTGGATATCTTTCCCGCTAGGGATACCTATCACCCTATGTCCGAGTATCCCACAGT GTTTTTCCTCGCCATGCTGGTCCTGATGGCCGTCCTGTATGTGCATATGCTCGCCAGAGCCTGTCAGCATGCCCCAAGGCATTGCCAGAAGCACAAACT

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CCTTCAGAAACACAGTGGAAGGCTATAGCGATCCCACAGGCAAATACGATCCCGCTGTGAGAAGCCTCCACAATCTGGCTCTGCCTTACTGGAACTTT  ${\tt GCCACAGGCAAAAACGTCTGCGATATCTGTACCGATGACCTCATGGGAAGCAGAAGCAATTTCGATAGCACAATCACAGACCAAGTGCCTTTCTCCGT\\$ TCGAGGATCCCTCCACCGATTACTATCAGGAACTGCAAAGGGGATATCTCCGAGATGAGCCCTTACGAAAAGGTCAGCGCTCGCCAATGGCGGAAGCTCC CTGTCCTACACAAACCCTGCCGCTGCCTCCCCCCAATCTGGCTTACGTCATCCCTATCGGAAACCTATGGCCAAATGAAAAAACCCAAAGCACACC TCAAGGGAGGCTCCGGCACATACTGTCTGAATAGGTATGGCTCCTTCTCCGTGACACTGGATATCGTCCAGGGAATCGAAAGCGCTGAGATTCTGCAA GCCGTCCCCTCCGGCGAAGGCGATCACCATGCCTTTGTGGATAGCATTTTCGAACAGTGGCTGCAAAGGCATAGGCCTCTGCAAGAGGTCTACCCTGA GGCTAACGCTCCCATTTGCACAGACGATCTGATGGGCTCCAGGTCCAACTTTGACTCCACCCTCATCTCCCCCAATAGCGTCTTCTCCCAGTGGAGGG AGCTATACCAATCCCGCTGTGGCTGCCGCTAGCGCTAACCTCGCCGCTGAGCATCCCACATGCGGATGCATTTTCAAAAACTTTAACCTCTTCCTCGC CCTCATCATTTGCAATGCCATTATCGATCCCCTCATCTATATGTCCCAGGTCCAGGGAAGCGCTAACGATCCCATTTTCCTCCTGCATCACGCTTTCG TCGACTCCATCTTTGAGCAATGGCTCCAGAGAAGGAATAGCATGAAGCTCCCCACACTGAAAGACATTAGGGATTGCCTCAGCCTCCAGAAATTCGAT AACCCTCCCTTTTTCCAAAACTCCCTGATTAGCAGAGCCCTCGTGGTCACCCATACCTATCTGGAACCCGGACCCGTCACCGCTCAGGTCGTGCTCCA GACCCGATGTGATTGGCGCTCTGCTCGGCGCGCTACCAAAGTGCCTAGGAATCAGGATTGGCTCGGCGTCAGCAGACAGCTCAGGACAAAGGCT GCCCTCGACGGAGGCAATAAGCATTTCCTCAGGAATCAGCCTCTGACATTCGCTCTGCAACTGCATGACCCCTAGCGGATACCTCGCCGAATGCGATGT GTGTACCGATCAGCTCTTCGGAGCCGCTAGGCCTGACGATCCCACACTGATTAGCAGAAACTCCAGGTTTAGCTCCTGGGAAGCCGCTATGCCTAGGG AAGACGCTCACTTTATCTATGGCTATCCCAAAAAAGGGACACGGGACACTCCTACACAACCGCTGAGGAAAGCCGCTACCGGAAAGTATGACCCTGCCGTC TCGCCAAAAAGAGAGTGCATCCCGATTACGTCACACACCCAACACTGGTTCTTTGCCTATCTGACACTGGCTAAGCATACCATTAGCTCCGACTAT GTGATTCCCATTGGCACATACGGACAGATGAAGAATGGCTCCGGCACAAACGTCCTGGAAACGCCTGTGATTCTGCTCCTGGAAGCCGGAGCCCTCGT GECTAGEGCTGCCGTCCTGCAACAGCTCGACAATGTGTGTGTGCTCGTGGCTCTGGCTATCGTCTACCTCATCGCTCTGGCTGTGTGTCAGTGTAGGA GAAAGAATTACGGACAGCTCGACATTTGCCCTCAGGAAGGCTTTGACCATAGGGATAGCAAAAGTGTCCCTGCAAGAGAAAAACTGTGAGCCTGTGGTC CCCAATGCCCTCCCGCTAGCGTCCTGTCCAGCCATAGCCCTGGCTCCGGCTCCAGCACAACCCAAGACGTCACCACAGACGTCACCACAGA GCCTGCCTCCGACGAATGGATGAAGAGATTCAATCCCCCTGCCGATGCCTGGCCCCAAGAGCTCGCCCCTATCGGACACAATAGGATGTACAATATGG TCGCCTTTCACTCCCAGGAACTGAGAAGGACACTGAAAGAGGTCCTGACATGCCTCCTGGGCTGCCTTTCTCCCACCAAGGCCCTGCCTTTGTGACATGG CATAGGTATCACCTCCTGTGTCTGGAAAGGGATCTGCAAAGGCTCATCGGAAACGGAAAGGCCTATGGTCCAGAGACTGCCTGAGGCTCAGGATGTGGC TCASTGTCTGGAAGTGGGACTGTTTGACACACCCCCTTTCTATAGCAATCAGGATCCCATTTTGGTCCTGCTCCACACATTCACAGACGCTGTGTTTG ACGAATGGCTCAGGAGATACAATGCCGATATCTCCACCTTTCTGGGAGCCGAAAGGGGTTAACGTCTGCGGAAGCCAACAGGGAAGGGGACAGTGTACC GAAGTGAGAGCCGATACCAGACCCTGGAGCGGATACAATTGCGGAGACTGTAAGTTTGGCTGGACCGGACCCAATTGCGAAAAGGGAAAAAGCCTCCCGT  ${\tt CATCAGACAGAATATCCATAGCCTCCTCCTCCTCAACGGAACCGGAGCCCAAACCCATCTGTCCAGCCAAGACCCTATCTTTGTGCTCCTGCATA}\\$ TATCACTCCGGCTGTAAGATTCTGCCTGGCGCTCAGGGACAGTTTCCCAGAGTGTGTATGACAGTGGATAAGCCTCGTGAATAAGGAATGCTGTCCCAG ACAGCTCCCCCATAGCTCCAGCCATTGGCTCAGGCTCCCCAGAATCTTTTGCTCCTGCCCTATCGGAGAGAATAGCCCTCTGCTCAGCGGAGACGGAG GCCCTTGCCCTAGCGGAGCTGGAGCCAAAAGAGATTTGTGTATGTGTGTAGGAAGACATGGGGACAGTATTGGCAAGTGCTCAACCAAGACTGGCTG TCACGAAGCCCCTGCCTTTCTGCCTTGGCATAGGCTCTTCCTCCTGAGATGGGAACAGGAAATCCAAGCCGCTATGACACCCGGAACCCAAAGCCCTT TETTTCTGCTCCTGCTCCTGACAGTGCTCGTGACAGGCTCCGGCCATGCCTCCGACAAAAGCCTCCACGTCGGCACACAGTGTGCCCTCACG AGAAGGTGTCCCCAAGAGGGGATTCGATCACAGAGACTCCCAAGGTCAGCCTCAACGTCACCTCCGGCTCCGGCTCCGGCTCCGGCTCCGCCTCCCACCCT CETECATAACEGAACCTCCECCACAGCCCACACCCCCCTCTGGAAGGCTTTGCCTCCCCCCTCACCGGAATCGCTGACGCTAGCCAAAGCTCCA TGCATAACGCTCTGCATATCTATATGAATGGCACAAGGGATACCCTCCTGGGACCCGGAAGGCCTTACAGGGCCATTGACTTTAGCCATCAGGGACCC GCTTTCGTCACCTGGCACAGATACCATGCCGCTATGCTCCTGGCTGTCTCTACTGTCTCTGGTCCTTCCAAACCTCCGCCGGACACTTTCCCAG AGCCTGTGTGTCCAGCAAAGCCTTTGAGCTCACCGTCAGCTGTCAGGGAGGCCTCCCCAAAGAGGCCTTGCATGGAGATTAGCTCCCCGGATGCCAAC CCCCTGCCCAAGTGGATGACAGAGAGTCCTGGCCTAGCGTCTTCTATAACAGAACCTGTCAGTGTAGCGGAAACTTTATGGGATTCAATTGCGGAAAC TGTGAGTCCGCCGAAATCCTCCAGGCTGTGCCTAGCGGAGAGGGGAGACGCTTTCGAACTGACAGTGTCCTGCCAAGGCGGACTGCCTAAGGAAACCGT CTGCGATAGCCTCGACGATTACAATCACCTCGTGACACTGTGTAACGGAACCTATGAGGGACTGCTCAGGAGAAACCAAATGGGACTGCTCAGCAATG CCCTCTGGGACCCCAATTCCCTTTCACAGGGGTCGACGATAGGGAAAGCTGGCCCTCCGTGTTTTACAATAGGACATACGAAAAGCTCAGCGCTGAG GAAACAGGATTTCTCCGTGCCTGGCATTGGCATTCTGACAGTGATTCTGGGAGTGCTCCTCCTCATCGGATGCTGGTACTGTAGGAGAAGGAATGGCT ATAGGGCTCTGATGTACTCCTACCTCCAGGATAGCGATCCCGATAGCTTTCAGGATTACATTAAGTCCTACCTCCAGCAAGCCTCCAGGATTTGGTCC TEGCTCCAGGGACAGGATGTGACACTGGCTCCCGCTACCGAACCCGCTAGCGGAAGCGCTGCCACATGGGGACAGGATGTGACAAGCGTCCCCGTCAC CTCCTGCGGAAGCTCCCCCGTCCCCGGAACCACAGACGGACACAGACCCACAGCCGAAGCCCCTAACACAGCGCTGGCCAAGTGCCTCTGGTCCACA CCCACAACCCTCCTGGTCGTCATGGCCACACTGGTCGCCCTCGTGGGACTGTTTGTGCTCCTGGCTTTCCTCACCACAACCGAATGGGTCGACACAAC CGCTAGGGAACTGCCTATCCCTGAGCCTGAGGGACCCGATGCCTCCAGCATTATGTCCACCGGAAGGCGCTGTGACACTGACAATCCTCCTGGGAATCT TITTCCTCTGCTGGGGCCCTTTCTTTCTGCACTCTGACACTGATTGTGCTCTGCCCCTCTGGGAGCCGCTATGGTCGGCGCTGTGCTCACCGCTCTGCTC GCCGGACTGGTCAGCCTCCTGTGTAGGCATAAGAGAAAGCAACTGCCTGGCGCTCTCGTCGCCAGAGCCGCTGTGCTCCAGCAACTGGATAACGTCAT CGATGTGATTACCTGTAGCTCCATGCTCAGCTCCCTGTGTATGACACCCCGAAAAGGTCCCCGTCAGCGAAGTGATGGGCACAACCCTCGCCGAAATGT  $\tt CCACCCCTGAGGCTACCGGAATGACACCCGCTCAGACAAGCGCTGGCCATTTCCCTAGGGCTTGCGTCAGCTCCAAGAATCTGATGGAGAAAGAGTGT\\$ TGCCCTCCCTGGAGCGGAGACAGAGCCCTCAGGTATCACTCCATCGTCACCCTCCCCAGAGCCCCTAGGGCTGTGGCTGCCATTTGGGTCGCCTCCGT GGTCTTCTCCACCTCTTCAGAGAGGGAACCATTAACGTCCACGATGTGGAAACCCAATTCAATCAGTATAAGACAGAGGCTGCCTCCAGGTATAACC TCACCATTAACCTCATGGAAAAGGAATGCTGTCCCCCTTGGTCCGGCGATAGGTCCCCCTGTGGCCAACTGTCCGGCAGAGGCTCCTGCCAAAACATT CCTCGCCTCCCACTCCACCAAAACCGATGCCTCCAGCACACACCATAGCTCCGTGCCTCCCCTCACCTCCAGCAATCACTCCAGCGAGCCGGAGTGC CTGGCTGGGGCATTGCCCTCCTGGTCCTGGTCCTGGTCCTGGTCGCCCATTGTGTATCTGATTGCCCTCTTCCTCGGCGCTATCGCTGTGGAT AGGTATATCTCCATCTTTTACGCTCTGAGATACCATAGCATTGTGACACTGCCTAGGGCTCCCAGACTGATTATGCCTGGCCAAGAGGCTGGCCTCGG CCAAGTGCCTCTGATTGTGGGAATCCTCTGGTCCTGATGGCCGTCGTCGTCGCCCTCCACCCTCGTGGCTCTGGTCGGCCTCTTCGTCCTGCTCGCCCT TTCTGCAATACAGAAGGCTCAGGAAAGGCTATACCCCTCTGATGGAGACACTGATTAGCCCTAACTCCGTGTTTAGCCAATGGAGAGTGGTCTGCGAT AGCCTCGAGGATTACGATACCCTCGGCACACTGTGTAACTCCCTGAATAGCACACCCCACAGCCCATCCCCAACTGGGACTGGCTGCCAATCAGACAGG CGCTAGGTGTCTGGAAGTGTCCATCTCCGACGGACACAGACCCCTCCAGGAAGTGTATCCCGAAGCCAATGCCCCTATCGGACACAATAGGGAAAGCT

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ATATGGTCCCCTTTATCCCTCTGTATGAGCCTAGCGGAACCACAAGCGTCCAGGTCCCACAACCGAAGTGATTAGCACAGCCCCTGTGCAAATGCCT
ACCGCTGAGTCCACCGGAAAGAAAAGGGTCCACCCTGACTATGTGATTACCACACAGCATTGGCTCGGCCTCCTGGGACCCCAATGGCACACAGCCTCA
GTTTGCCAATCTGCATCAGATTCTGAAAGGCGGAACCGGAACCTATTGCCTCAACGTCAGCCTCGCCGATACCAATAGCCTCGCCGTCGTGTCCACCC
AACCCGAACCCTGACGCCTAGCTCCATCATGAGCACAGAGTCCATCACAGCCTCCCTGGACCCCTCCTGGATGGCACAGCCACAAGCATT
ACCGGAAGCCTCGGCCCTCTGGTCGACCGCTACCCTCAGGCTCGTGAAAAGGCAAGTCCTTTGGATTGGCTCTTGTTTGAACTGTTGGAGAGG
CGGACAGGTCAGCTCAAGGTCAGCAATGACGGACCCACACTGATTGGCGTTAGCTTTAGCATTTGCCCTC

Melanoma cancer Specific Savine Scramble process Scramble - Output File Scramble version: 0.1 beta, 08/02/1999 Num. genes : 10 Num. segments : 121 Segment length : 30 Segment overlap : 15 Segments in original order: : BAGE Gene Segment# : 1 Offset : 1 1st Codon : 1 AAMAARAVFLALSAQLLQARLMKEESPVVS : BAGE Gene Segment# : 2 Offset : 16 1st Codon : 1 LLQARLMKEESPVVSWRLEPEDGTALCFIF CTGCTCCAGGCTAGGATAGAGAGGAAAGCCCTGTGGTCAGCTGGAGGCTCGAGCCTGAGGATGGCACAGCCCTCTGCTTTATCTTT Gene : BAGE Segment# : 3 Offset : 31 1st Codon : 1 WRLEPEDGTALCFIFAA TGGAGACTGGAACCCGAAGACGGAACCGCTCTGTGTTTCATTTTCGCTGCC : GAGE-1 Gene Segment# : 1 Offset : 1 1st Codon : 1 A A M S W R G R S T Y R P R P R R Y V E P P E M I G P M R P GCCGCTATGTCCTGGAGAGGCAGAAGCACATACAGACCCAGACCCAGAAGGTATGTGGAACCCCTGAGATGATCGGACCCATGAGGCCT Gene : GAGE-1 Segment# : 2 Offset : 16 1st Codon : 1 RRYVBPPBMIGPMRPEQPSDEVBPATPEEG AGGAGATACGTCGAGCCTCCCGAAATGATTGGCCCTATGAGACCCGAACAGTTTAGCGATGAGGTCGAGCCTGCCACACCCGAAGAGGGA Gene : GAGE-1 Segment# : 3 Offset : 31 1st Codon : 1 EQFSDBVEPATPEEGEPATQRQDPAAAQEG GAGCAATTCTCCGACGAAGTGGAACCCGCTACCCCTGAGGAAGGCGAACCCGCTACCCAAAGGCAAGACCCTGCCGCTGCCCCAAGAGGGA Gene : GAGE-1 Segment# : 4 Offset : 46 1st Codon : 1 E PATQRQDPAAAQEGEDEGASAGOGPKPBA GAGCCTGCCACAGAGACAGGATCCCGCTGCCGCTCAGGAAGGCGAAGACGAAGGCGCTAGCGCTAGGCCTAAGGCCTTAAGCCTGAGGCT : GAGE-1 Gene Segment# : 5 Offset : 61 1st Codon : 1

Figure 27 (Cont)

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B D E G A S A G Q G P K P E A D S Q E Q G H P Q T G C E C E GAGGATGAGGGAGCCTCCGCCGGACAGGGGACCCAAACCCGAAGCCGATAGCCAAGAGCAAGGCCATCCCCAAACCGGATGCGAATGCGAA : GAGE-1 Segment# : 6 Offset : 76 1st Codon : 1 D S Q E Q G H P Q T G C E C E D G P D G Q E M D P P N P E E GACTCCCAGGAACAGGGACACCCTCAGACAGGCTGTGAGTGTGAGGATGGCCCTGACGGACAGGAAATGGATCCCCCTAACCCTGAGGAA Gene : GAGE-1 Segment# : 7 Offset : 91 1st Codon : 1 D G P D G .Q B M D P P N P E B V K T P E B B M R S H Y V A Q GACGGACCCGATGGCCAAGAGATGGACCCTCCCAATCCCGAAGAGGGTCAAGACACCCGAAGAGGAAATGAGAAGCCATTACGTCGCCCAA : GAGE-1 Gene Segment# : 8 Offset : 106 1st Codon : 1 V K T P E E E M R S H Y V A Q T G I L W L L M N N C F L N L GTGAAAACCCCTGAGGAAGAGATGAGGTCCCACTATGTGGCTCAGACAGGCATTCTGTGGCTGCTCATGAATAACTGTTTCCTCAACCTC Gene : GAGE-1 Segment# : 9 Offset 1st Codon : 1 TGILWLLNNNCFLNLSPRKPAA ACCEGAATCCTCTGGCTCCTGATGAACAATTGCTTTCTGAATCTGTCCCCCAGAAAGCCTGCCGCT Gene : gp100In4 Segment# : 1 Offset : 1 1st Codon : 1 A A S W S Q K R S P V Y V W K T W G E G L P S Q P I I H T C GCCGCTAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGAGAGGGACTGCCTAGCCAACCCATTATCCATACCTGT Gene : gpl00In4 Segment# : 2 Offset : 16 1st Codon : 1 TWGEGLPSQPIIHTCVYFPLPDHLSFGRPF ACCTGGGGGGAAGGCCTCCCCTCCCAGCCTATCATTCACACATGCGTCTACTTTTTCCTCCCCGATCACCTCAGCTTTGGCAGACCCTTT Gene : gp100In4 Segment# : 3 Offset : 31 1st Codon : 1 V Y F P L P D H L S F G R P F H L N F C D P L A A GTGTATTTCTTCTGCCTGACCATCTGTCCTTCGGAAGGCCTTTCCATCTGAATTTCTGTGACTTTCTGGCTGCC Gene : MAGE-1 Segment# : 1 Offset 1st Codon : 1 AAMSLEQRSLHCKPBBALBAQQBALGLVCV GCCGCTATGTCCCTGGAACAGAGAAGCCTCCACTGTAAGCCTGAGGAAGCCCTCGAGGCTCAGCAAGAGGCTCTGGGACTGGTCTCCGTC Gene : MAGE-1 Segment# : 2 Offset E A L E A Q Q E A L G L V C V Q A A T S S S P L V L G T L : MAGE-1 Gene Segment# : 3 Offset : 31 Q A A T S S S P L V L G T L B B V P T A G S T D P P Q S P CAGGCTGCCACAGCTCCAGCTCCCCCTCGTGCTCGGCCACACGGCACAGAGCACCACAGAGCACAGAGCCCTCCCCAAAGCCCT

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Gene : MAGE-1 Segment# : 4 Offset : 46 1st Codon : 1 E E V P T A G S T D P P Q S P Q G A S A F P T T I N F T R Q : MAGE-1 Gene Segment# : 5 Offset : 61 1st Codon : 1 Q G A S A F P T T I N F T R Q R Q P S E G S S S R E E E G P Gene : MAGE-1 Segment# : 6 Offset 1st Codon : 1 RQPSEGSSSREEEGPSTSCILESLFRAVIT AGGCAACCCTCCGAGGGAGCTCCAGCAGAGAGGGAAGAGGGACCCTCCACCTCCTGCATTCTGGAAAGCCTCTTCAGAGCCGTCATCACA : MAGE-1 Gene Segment# : 7 Offset : 91 1st Codon : 1 S T S C I L E S L F R A V I T K K V A D L V G F L L L K Y R AGCACAAGCTGTATCCTCGAGTCCCTGTTTAGGGCTGTGATTACCAAAAAGGTCGCCGATCTGGTCGGCTTTCTGCTCCTGAAATACAGA : MAGE-1 Gene Segment# : 8 1st Codon : 1 K K V A D L V G F L L L K Y R A R E P V T K A B M L B S V I AAGAAAGTGGCTGACCTCGTGGGATTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGGAAATGCTCGAGTCCGTGATT : MAGE-1 Gene Segment# : 9 Offset : 121 1st Codon : 1 ARBPVTKAEMLESVIKNYKHCFPEIFGKAS GCCAGAGAGCCTGTGACAAAGGCTGAGATGCTGGAAAGCGTCATCAAAAACTATAAGCATTGCTTTCCCGAAATCTTTGGCAAAGCCTCC Gene : MAGE-1 Segment# : 10 Offset : 136 1st Codon : 1 K N Y K H C P P B I F G K A S E S L Q L V F G I D V K R A D AAGAATTACAAACACTGTTTCCCTGAGATTTTCGGAAAGGCTAGCGAAAGCCTCCAGCTCGTGTTTGGCATTGACGTCAAGGAAGCCGAT Gene : MAGE-1 Segment# : 11 Offset : 151 1st Codon : 1 ESLQLVFGIDVKEADPTGHSYVLVTCLGLS GAGTCCCTGCAACTGGTCTCCGGAATCGATGTGAAAGAGGCTGACCCTACCGGCACACTCCTACGTCCTCGCTCACCTGTCTCGGGACTGTCC Gene : MAGE-1 Segment# : 12 : 166 1st Codon : 1 PTGHSYVLVTCLGLSYDGLLGDNQIMPKTG CCCACAGGCCATAGCTATGTGCTCGTGACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGGATAACCAAATCATGCCCAAAACCGGA : MAGE-1 Segment# : 13 Offset : 181 1st Codon : 1 Y D G L L G D N Q I M P K T G F L I I V L V M I A M E G G H : MAGE-1 Gene

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Segment# : 14 : 196 1st Codon : 1 F L I I V L V M I A M E G G H A P E E E I W E E L S V M E V TTCCTCATCATTGTGCTCGTGATGATCGCTATGGAAGGCGGACCCCCCGAAGAGGAAATCTGGGAGGAACTGTCCGTGATGGAGGTC : MAGE-1 Segment# : 15 Offset : 211 1st Codon : 1 A P E E E I W E E L S V M E V Y D G R E H S A Y G E P R K L GCCCCTGAGGAAGAGATTTGGGAAGAGCTCAGCGTCATGGAAGTGTATGACGGAAGGGAACACTCCGCCTATGGCGAACCCAGAAAGCTC : MAGE-1 Gene Segment# : 16 Offset : 226 1st Codon : 1 Y D G R E H S A Y G E P R K L L T Q D L V Q E K Y L E Y R O TACGATGGCAGAGAGCATAGGGCTTACGGAGAGCCTAGGAAACTGCTCACCCAAGACCTCGTGCAAGAGAAATACCTCGAGTATAGGCAA : MAGE-1 Gene Segment# : 17 : 241 Offset 1st Codon : 1 L T Q D L V Q B K Y L B Y R Q V P D S D P A R Y B F L W G P : MAGE-1 Gene Segment# : 18 Offset : 256 1st Codon : 1 V P D S D P A R Y E F L W G P R A L A E T S Y V K V L E Y V GTGCCTGACTCCGACCCTGCCAGATACGAATTCCTCTGGGGACCCAGAGCCCTCGCGAAACCTCCTACGTCAAGGTCCTGGAATACGTC Gene : MAGE-1 Segment# : 19 Offset : 271 1st Codon : 1 RALAETSYVKVLEYVIKVSARVRFFFF<sub>SLR</sub> : MAGE-1 Gene Segment# : 20 Offset : 286 1st Codon : 1 I K V S A R V R F P P P S L R E A A L R E B E E G V A A ATCAAAGTGTCCGCCAGAGTGAGATTCTTTTTCCCTAGCCTCAGGGAAGCCGCTCTGAGAGAGGAGGAGGAGGCCGTCGCCGCT : MAGE-3 Gene Segment# : 1 Offset : 1 1st Codon : 1 AAM PLEQRSQHCKPEEGLEARGEALGLVGA GCCGCTATGCCTCTGGAACAGAGAGACCCAACACTGTAAGCCTGAGGAAGGCCTCGAGGCTAGGGGAGAGGCTCTGGGACTGGTCGGCCCT Gene : MAGE-3 Segment# : 2 Offset : 16 1st Codon : 1 EGLEARGEALGLVGAQAPATEEQEAASSSS GAGGGACTGGAAGCCAGAGGCCGAAGCCCTCGTCGGAGCCCCAAGCCCCTGCCACAGAGGAACAGGAAGAGCCGCTAGCTCCAGCTCC Gene : MAGE-3 Segment# : 3 Offset : 31 Q A P A T B B Q B A A S S S S T L V B V T L G E V P A A B S Gene : MAGE-3 Segment# : 4 Offset

### 187/216

1st Codon : 1 T L V E V T L G E V P A A E S P D P P Q S P Q G A S S L P T ACCUTCGTGGAAGTGACACTGGGAGAGGTCCCCGCTGCCGAAAGCCCTGACCCTCCCCAAAGCCCTCAGGGAGCCTCCAGCCTCCCCACA Gene : MAGE-3 Segment# : 5 Offset : 61 1st Codon : 1 P D P P Q S P Q G A S S L P T T M N Y P L W S Q S Y E D S S : MAGE-3 Segment# : 6 Offset : 76 1st Codon : 1 T M N Y P L W S Q S Y E D S S N Q E E G P S T F P D L E S ACCATGAACTATCCCCTCTGGTCCCAGTCCTACGAAGACTCCAGCAATCAGGAAGAGGAGGAGGCCCTAGCACATTCCCTGACCTCGAGTCC Segment# : 7 Offset : 91 1st Codon : 1 N Q B B B G P S T P P D L B S E P Q A A L S R K V A B L V H AACCAAGAGGGAAGAGGGACCCTCCACCTTTCCCGATCTGGAAAGCGGAATTCCAAGCCGCTCTGTCCAGGAAAGTGGCTGAGCTCGTGCAT : MAGE-3 Segment# : 8 Offset : 106 1st Codon : 1 B F Q A A L S R K V A E L V H F L L L K Y R A R E P V T K A GAGTTTCAGGCTGCCCTCAGCAGAAAGGTCGCCGAACTGGTCCACTTTCTGCTCCTGAAATACAGAGCCAGAGAGCCTGTGACAAAGGCT : MAGE-3 Segment# : 9 Offset : 121 1st Codon : 1 PLL L K Y R A R E P V T K A E M L G S V V G N N Q Y P P : MAGE-3 Segment# : 10 Offset : 136 1st Codon : 1 B M L G S V V G N W Q Y P P P V I F S K A S S S L Q L V F G : MAGE-3 Gene Segment# : 11 Offset : 151 1st Codon : 1 VIFSKASSSLQLVPGIELMBVDPIGHLYIP GTGATTTTCTCCAAGGCTAGCCTCCAGCCTCCAGCTCGTGTTTGGCATTGAGCTCATGGAAGTGGATCCCATTGGCCATCTGTATATCTTT : MAGE-3 Gene Segment# : 12 Offset : 166 lst Codon : 1 I B L M B V D P I G H L Y I F A T C L G L S Y D G L L G D N ATCGAACTGATGGAGGTCGACCCTATCGGACACCTCTACATTTTCGCTACCTGTCTGGGACTGTCCTACGATGGCCTCCTGGGAGACAAT Gene : MAGE-3 Segment# : 13 Offset : 181 1st Codon : 1 A T C L G L S Y D G L L G D N Q I M P K A G L L I I V L A I GCCACATGCCTCGGCCTCAGCTATGACGGACTGCTCGGCGGATAACCAAATCATGCCCAAAGCCGGACTGCTCATCATTGTGCTCGCCATT Gene : MAGE-3 Segment# : 14 Offset : 196 1st Codon : 1 Q I M P K A G L L I I V L A I I A R E G D C A P E B K I W B

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CAGATTATGCCTAAGGCTGGCCTCCTGATTATCGTCCTGGCTATCATTGCCAGAGAGGGGAGACTGTGCCCCTGAGGAAAAGATTTGGGAA
        : MAGE-3
Gene
Segment# : 15
Offset
       : 211
 1st Codon : 1
 I A R E G D C A P E E K I W E E L S V L E V F E G R E D S I
\tt ATCGCTAGGGAAGGCGATTGCGCTCCCGAAGAGAAAATCTGGGAGGAACTGTCCGTGCTCGAGGTCTTCGAAGGCAGAGAGGATAGCATT
Gene
        : MAGE-3
Segment# : 16
       : 226
1st Codon : 1
 ELSVLEVFEGREDSILG'DPKKLLTQHFVQE
GAGCTCAGCGTCCTGGAAGTGTTTGAGGGAAGGGAAGACTCCATCCTCGGCGATCCCAAAAAGCTCCTGACACAGCATTTCGTCCAGGAA
        : MAGE-3
Segment# : 17
Offset
       : 241
1st Codon : 1
 LGDPKKLLTQHPVQBNYLBYRQVPGSDPAC
: MAGE-3
Segment# : 18
       : 256
Offset
1st Codon : 1
 NYLEYRQVPGSDPACYEFLWGPRALVETSY
AACTATCTGGAATACAGACAGGTCCCCGGAAGCGATCCCGCTTGCTATGAGTTTCTGTGGGGCCCTAGGGCTCTGGTCGAGACAAGCTAT
Gene
       : MAGE-3
Segment# : 19
Offset
       : 271
1st Codon : 1
 Y E F L W G P R A L V E T S Y V K V L H H M V K I S G G P H
TACGAATTCCTCTGGGGACCCAGAGCCCTCGTGGAAACCTCCTACGTCAAGGTCCTGCATCACATGGTGAAAATCTCCGGCGGACCCCAT
Gene
       : MAGE-3
Segment# : 20
Offset
       : 286
1st Codon : 1
V K V L H H M V K I S G G P H I S Y P P L H E W V L R E G E
GTGAAAGTGCTCCACCATATGGTCAAGATTAGCGGAGGCCCTCACATTAGCTATCCCCCTCTGCATGAGTGGGTGCTCAGGGAAGGCGAA
Gene
       : MAGE-3
Segment# : 21
Offset
1st Codon : 1
I S Y P P L H E W V L R E G E E A A
ATCTCCTACCCTCCCCTCCACGAATGGGTCCTGAGAGGGGAGAGGGGAAGCCGCT
       : PRAME
Gene
Segment# : 1
       : 1
Offset
1st Codon : 1
AAMERRRLWGSIQSRYISMSVWTSPRRLVE
GCCGCTATGGAAAGGAGGAAGGCTCTGGGGAAGCATTCAGTCCAGGTATATCTCCATGTCCGTGTGGACCTCCCCCAGAAGGCTCGTGGAA
Gene
       : PRAME
Segment# : 2
Offset
       : 16
1st Codon : 1
Y I S M S V W T S P R R L V E L A G Q S L L K D E A L A I A
TACATTAGCATGAGCGTCTGGACAAGCCCTAGGAGACTGGTCGAGCTCGCCGGACAGTCCCTGCTCAAGGATGAGGCTCTGGCTATCGCT
Gene
       : PRAME
Segment# : 3
Offset
      : 31
1st Codon : 1
LAGQSLLKDEALAIAALELLPRELFP<sub>M</sub>
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: PRAME Gene Segment# : 4 Offset : 46 1st Codon : 1 ALELL PRELPPPLPMAAFDGRHSQTLKAM V GCCCTCGAGCTCCTGCCTAGGGGAACTGTTTTCCCCCTCTGTTTATGGCTGCCTTTGACGGAAGGCATAGCCAAAACCCTCAAGGCTATGGTC : PRAME Segment# : 5 Offset : 61 1st Codon : 1 A A F D G R H S Q T L K A M V Q A W P F T C L P L G V L M K GCCGCTTTCGATGGCAGACACTCCCAGACACTGAAAGCCATGGTGCAAGCCTGGCCCTTTACCTGTCTGCCTCTGGGAGTGCTCATGAAA Gene : PRAME Segment# : 6 Offset : 76 Q A W P F T C L P L G V L M K G Q H L H L E T F K A V L D G CAGGCTTGGCCTTTCACATGCCTCCCCCTCGGCGTCCTGATGAAGGGACAGCATCTGCATCTGGAAACCTTTAAGGCTGTGCTCGACGGA Gene : PRAME Segment# : 7 Offset : 91 1st Codon : 1 G Q H L H L E T F K A V L D G L D V L L A Q E V R P R R W K GGCCAACACCTCCACCTCGAGACATTCAAAGCCGTCCTGGATGGCCTCGACGTCCTGCTCGCCCAAGAGGTCAGGCCTAGGAGATGGAAA : PRAME Gene Segment# : 8 Offset : 106 1st Codon : 1 LDVLLAQBVRPRRWKLQVLDLRKNSH<sub>QDFW</sub> Gene : PRAME Segment# : 9 Offset : 121 1st Codon : 1 LQVLDLRKNSHQDFWTVWSGNRASLYSFPE CTGCAAGTGCTCGACCTCAGGAAAAACTCCCACCAAGACTTTTGGACAGTGTGGAGCGGAAACAGAGCCTCCCTGTATAGCTTTCCCGAA : PRAME Segment# : 10 Offset : 136 1st Codon : 1 T V W S G N R A S L Y S P P B P E A A Q P M T K K R K V D G ACCOTCTGGTCCGGCAATAGGGCTAGCCTCTACTCCTTCCCTGAGGCTGAGGCTGCCCCAACCCATGACCAAAAAGAGAAAGGTCGACGGA : PRAME Segment# : 11 Offset : 151 1st Codon : 1 PEAAQPMTKKRKVDGLSTEAEQPFIPVEV<sub>L</sub> CCCGAAGCCGCTCAGCCTATGACAAAGAAAAGGAAAGTGGATGGCCTCAGCACAGAGGCTGAGCAACCCTTTATCCCTGTGGAAGTGCTC Gene ' : PRAME Segment# : 12 Offset : 166 1st Codon : 1 LSTEAEQPPIPVEVLVDLFLKEGACDELFS Gene : PRAME Segment# : 13 Offset : 181 1st Codon : 1 V D L P L K B G A C D B L P S Y L I B K V K R K K N V L R L GTGGATCTGTTTCTGAAAGAGGGGAGCCTGTGACGAACTGTTTAGCTATCTGATTGAGAAAGTGAAAAGGAAAAAGAATGTGCTCAGGCTC Gene : PRAME Segment# : 14

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Offset : 196 1st Codon : 1 Y L I B K V K R K K N V L R L C C K K L K I P A M P M Q D I TACCTCATCGAAAAGGTCAAGAGAAAAGAAAAACGTCCTGAGACTGTGTTGCAAAAAGCTCAAGATTTTCGCTATGCCTATGCAAGACATT Gene : PRAME Segment# : 15 Offset : 211 1st Codon : 1 C C K K L K I F A M P M Q D I K M I L K M V Q L D S I R D L TGCTGTAAGAAACTGAAAATCTTTGCCATGCCCATGCAGGATATCAAAATGATTCTGAAAATGGTCCAGCTCGACTCCATCGAAGACCTC Gene : PRAME Segment# : 16 Offset : 226 1st Codon : 1 K M I L K M V Q L D S I E D L E V T C T W K L P T L A K P S AAGATGATCCTCAAGATGGTGCAACTGGATAGCATTGAGGATCTGGAAGTGACATGCACATGGAAACTGCCCTACCCTACCCTACCCAAATTCTCC : PRAME Gene Segment# : 17 : 241 1st Codon : 1 EVTCTWKLPTLAKFSPYLGQMINLRRLLLS GAGGTCACCTGTACCTGGAGGCTCCCCACACTGGCTAAGTTTAGCCCTTACCTCGGCCAAATGATTAACCTCAGGAGACTGCTCCTGTCC : PRAME Gene Segment# : 18 Offset : 256 1st Codon : 1 PYLGQMINLRRLLLSHIHASSYISPEKEEQ CCCTATCTGGGACAGATGATCAATCTGAGAAGGCTCCTGCTCAGCCATATCCATGCCTCCAGCTATATCTCCCCCGAAAAGGAAGAGCAA Gene : PRAME Segment# : 19 : 271 1st Codon : 1 HIHASSYISPEKEEQYIAQPTSQFLSLQCL CACATTCACGCTAGCTCCTACATTAGCCCTGAGAAAGAGGAACAGTATATCGCTCAGTTTACCTCCCAGTTTCTGTCCCTGCAATGCCTC Gene : PRAME Segment# : 20 Offset : 286 1st Codon : 1 Y I A Q F T S Q F L S L Q C L Q A L Y V D S L F F L R G R L TACATTGCCCAATTCACAAGCCAATTCCTCAGCCTCCAGTGTCTGCAAGCCCTCTACGTCGACTCCCTGTTTTTCCTCAGGGGAAGGCTC Gene : PRAME Segment# : 21 Q A L Y V D S L P P L R G R L D Q L L R H V M N P L B T L S CAGGCTCTGTATGTGGATAGCCTCTTCTTTCTGAGAGGCAGACTGGATCAGCTCCTGAGACACGTCATGAATCCCCTCGAGACACTGTCC Gene : PRAME Segment# : 22 Offset : 316 1st Codon : 1 D Q L L R H V M N P L B T L S I T N C R L S E G D V M H L S GACCAACTGCTCAGGCATGTGATGAACCCTCTGGAAACCCTCAGCATTACCAATTGCAGACTGTCCGAGGGAGACGTCATGCATCTGTCC Gene : PRAME Segment# : 23 Offset : 331 I T N C R L S B G D V M H L S Q S P S V S Q L S V L S L S G ATCACAAACTGTAGGCTCAGCGAAGGCGATGTGATGCACCTCAGCCAAAGCCCTAGCGTCAGCCAACTGTCCGTGCTCAGCCTCAGCGGA : PRAME Gene Segment# : 24 Offset : 346

Figure 27 (Cont)

1st Codon : 1

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Q S P S V S Q L S V L S L S G V M L T D V S P E P L Q A L L CAGTCCCCTCCGTGTCCCAGCTCAGCGTCCTGTCCCGGCGTCATGCTCACCGATGTGTCCCCCGAACCCCTCCAGGCTCTGCTC : PRAME Segment# : 25 Offset : 361 1st Codon : 1 V M L T D V S P E P L Q A L L B R A S A T L Q D L V F D B C GTGATGCTGACAGACGTCAGCCCTGAGCCTCTGCAAGCCCTCCTGGAAAGGGCTAGCCCTACCCTCCAGGATCTGGTCTTCGATGAGTGT Gene : PRAME Segment# : 26 : 376 Offset 1st Codon : 1 E R A S A T L Q D L V P D E C G I T D D Q L L A L L P S L S GAGAGAGCCTCCGCCACACTGCAAGACCTCGTGTTTGACGAATGCGGAATCACAGACGATCAGCTCCTGGCTCTCCCTGCCCTGTCC : PRAME Gene Segment# : 27 Offset : 391 1st Codon : 1 G I T D D Q L L A L L P S L S H C S Q L T T L S F Y G N S I GGCATTACCGATGACCAACTGCTCGCCCTCCCTGCCTAGCCTCAGCCATTGCTCCCAGCTCACCACCTGTCCTTCTATGGCAATAGCATT Gene : PRAME Segment# : 28 Offset 1st Codon : 1 H C S Q L T T L S P Y G N S I S I S A L Q S L L Q H L I G L CACTGTAGCCAACTGACAACCCTCAGCTTTTACGGAAACTCCATCTCCATCTCCGCCCCTCCAGTCCCTGCTCCAGCATCTGATTGGCCTC : PRAME Gene Segment# : 29 Offset : 421 1st Codon : 1 S I S A L Q S L L Q H L I G L S N L T H V L Y P V P L E S Y AGCATTAGCGCTCTGCAAAGCCTCCTGCAACACCTCATCGGACTGTCCAACCTCACCCATGTGCTCTACCCTGTGCCTCTGGAAAGCTAT Gene : PRAME Segment# : 30 Offset : 436 1st Codon : 1 S N L T H V L Y P V P L E S Y E D I H G T L H L E R L A Y L AGCAATCTGACACGTCCTGTATCCCGTCCCCTCGAGTCCTACGAAGACATTCACGGAACCCTCCACCTCGAGAGACTGGCTTACCTC Gene : PRAME Segment# : 31 : 451 Offset 1st Codon : 1 E D I H G T L H L E R L A Y L H A R L R E L L C E L G R P S GAGGATATCCATGGCACACTGCATCTGGAAAGGCTCGCCTATCTGCATGCCAGACTGAGAGAGCTCCTGTGTGAGCTCGGCAGACCCTCC Gene : PRAME Segment# : 32 Offset 1st Codon : 1 HARLREL CELGRPS M V W L S A N P C P H C G D R CACGCTAGGCTCAGGGAACTGCTGTGCGAACTGGGAAGGCCTAGCATGGTGTGCGTGTCCGCCAATCCCTGTCCCCATTGCGGAGACAGA Gene : PRAME Segment# : 33 Offset : 481 1st Codon : 1 M V W L S A M P C P H C G D R T P Y D P E P I L C P C P M P ATGGTCTGGCTCAGCGCTAACCCTTGCCCTCACTGTGGCGATAGGACATTCTATGACCCTGAGCCTATCCTCTGCCCTTGCTTTATGCCT Gene : PRAME Segment# : 34 Offset : 496 1st Codon : 1 TPYDPEPILCPCFMPNAA ACCTTITACGATCCCGAACCCATTCTGTGTCCCTGTTTCATGCCCCAATGCCGCT

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Gene : TRP2IN2 Segment# : 1 Offset 1st Codon : 1 A A L M E T H L S S K R Y T E E A G G P P P W L K V Y Y Y R GCCGCTCTGATGGAGACACACCTCAGCTCCAAGAGATACACAGAGGGAAGCCGGAGGCTTTTTCCCTTGGCTCAAGGTCTACTATTACAGA Gene : TRP2IN2 Segment# : 2 Offset : 16 EAGGPPP W L K V Y Y Y R P V I G L R V W O W E V I S C GAGGCTGGCGGATTCTTTCCCTGGCTGAAAGTGTATTACTATAGGTTTGTGATTGGCCTCAGGGTCTGGCAATGGGAAGTGATTAGCTGT Gene : TRP2IN2 Segment# : 3 : 31 Offset 1st Codon : 1 FVIGLRVWQWEVISCKLIKRATTROPAA TTCGTCATCGGACTGAGAGTGTGGCAGTGGGAGGTCATCTCCTGCAAACTGATTAAGAGAGCCACAACCAGACAGCCTGCCGCT : NYNSOla Gene Segment# : 1 Offset 1st Codon : 1 A A M Q A E G R G T G G S T G D A D G P G G P G I P D G P G GCCGCTATGCAAGCCGAAGGCAGAGGCACAGGCGGAAGCACAGGCGATGCCCGATGGCCCTGGCGGACCCGGAATCCCTGACGGACCCGGA Gene : NYNSOla Segment# : 2 Offset D A D G P G G P G I P D G P G G N A G G P G E A G A T G G R GACGCTGACCGGACCCCGGGCCTTGCCGATGCCCTGGCGGAAACGCTGGCGGACCCGGAGAGGCTGGCGCTACCGGAGGCAGA : NYNSOla Gene Segment# : 3 Offset : 31 1st Codon : 1 G N A G G P G B A G A T G G R G P R G A G A A R A S G P G G : NYNSOla Gene Segment# : 4 Offset : 46 1st Codon : 1 G P R G A G A A R A S G P G G G A P R G P H G G A A S G L N GGCCCTAGGGGAGCCGGCCGCTAGGCGCACCCGGAGCCCGAGGCCGCTAGGGGAGCCCCTAGGGGAGCCGCTAGCGGACTGAAT Gene : NYNSOla Segment# : 5 Offset : 61 1st Codon : 1 GAPRGPHGGAASGLNGCCRCGARGPESRLL GECCTCCCAGAGGCCCTCACGGAGGCCCTGCCTCCGGCCTCAACGGATGCTGTAGGTGTGCGCGTAGGGGACCCGAAAGCAGACTGCTC Gene : NYNSOla Segment# : 6 Offset 1st Codon : 1 G C C R C G A R G P E S R L L E F Y L A M P P A T P M E A E GGCTGTTGCAGATGCGGAGCCAGAGGCCCTGAGTCCAGGCTCCTGGAATTCTATCTGGCTATGCCTTTCGCTACCCCTATGGAAGCCGAA Gene : NYNSOla Segment# : 7 Offset 1st Codon : 1 GAGTTTTACCTCGCCATGCCCTTTGCCACACCCATGGAGGCTCGCCAGAAGGTCCCTTGGCTAGGATGCCCCTCCCCCTCCCCGTC Gene : NYNSOla

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Segment# : 8 Offset : 106 LARRSLAQDAPPLPVPGVLLKEFTVSGNIL Gene : NYNSOla Segment# : 9 Offset : 121 1st Codon : 1 PGVLLKEFTVSGNILTIRLTAADHRQLQLS CCCGGAGTGCTCCTGAAAGAGTTTACCGTCAGCGGAAACATTCTGACAATCAGACTGACGCCGCTGACCATAGGCAACTGCAACTGTCC : NYNSOla Segment# : 10 Offset : 136 1st Codon : 1 TIRLTAADHRQLQLSISSCLQQLSLLMWIT ACCATTAGGCTCACCGCTGCCGATCACAGACAGCTCCAGCTCAGCCATTAGCTCCTGCCTCCAGCAACTGTCCCTGCTCATGTGGATCACA Gene : NYNSOla Segment# : 11 Offset : 151 1st Codon : 1 ISSCLQQLSLLMWITQCFLPVFLAQPPSGO : NYNSO1a Gene Segment# : 12 Offset : 166 1st Codon : 1 QCFLPVFLAQPPSGQRAA CAGTGTTTCCTCCCCGTCTTCCTCGCCCAACCCCCTAGCGGACAGAGAGGGCTGCC Gene : NYNSO1b Segment# : 1 Offset 1st Codon : 1 A A M L M A Q E A L A F L M A Q G A M L A A Q E R R V P R A GCCGCTATGCTCATGGCTCAGGAAGCCCTCGCCTTTCTGATGGCCCAAGGCGCTATGCTCGCCGCTCAGGAAAGGAGAGTGCCTAGGGCT : NYNSO1b Segment# : 2 Offset : 16 1st Codon : 1 Q G A M L A A Q B R R V P R A A B V P G A Q G Q Q G P R G R CAGGGAGCCATGCTGGCTGCCCAAGAGAGAAGGGTCCCCAGAGCCGCTGAGGTCCCCGGAGCCCAAGGCCAACAGGGACCCAGAGGCAGA : NYNSO1b Segment# : 3 Offset : 31 1st Codon : 1 A E V P G A Q G Q Q G P R G R E B A P R G V R M A A R L Q G GCCGAAGTGCCTGGCGCTCAGGGACAGCCAAGGCCCTAGGGGAAGGGGAAGAGGCTCCCAGAGGCGTCAGGATGGCCGCTAGGCTCCAGGGA : NYNSO1b Gene Segment# : 4 Offset : 46 1st Codon : 1 EEAPRGVRMAARLQGAA GAGGAAGCCCCTAGGGGAGTGAGAATGGCTGCCAGACTGCAAGGCGCTGCC : LAGE1 Gene Segment# : 1 Offset A A M Q A B G Q G T G G S T G D A D G P G G P G I P D G P G GCCGCTATGCAAGCCGAAGGCCAAGGCACAGGCGGAAGCACAGGCGATGCCGATGCCCTGGCGGACCCGGAATCCCTGACGGACCCGGA Gene : LAGE1 Segment# : 2 Offset : 16

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1st Codon : 1 DADGPGGPGIPDGPGGNAGGPGBAGATGGR GACGCTGACGGACCCGGAGGCCCTGGCATTCCCGATGGCCCTGGCGGAAACGCTGGCGGAGACGCCGGAGAGGCTGGCGCTACCGGAGGCAGA Gene : LAGE1 Segment# : 3 Offset 1st Codon : 1 G N A G G P G E A G A T G G R G P R G A G A A R A S G P R G GGCANTGCCGGAGGCCCTGGCGAAGCCGCAGGCCACAGGGGGAAGGGGGACCCAGAGGCGCTGGCGAGAGCCTCCGGCCCTAGGGGA Segment# : 4 Offset : 46 1st Codon : 1 G P R G A G A A R A S G P R G G A P R G P H G G A A S A Q D GGCCCTAGGGGAGCCGGAGCCGCTAGGGCTAGCGGACCCAGAGGCGGAGCCCCTAGGGGACCCCATGGCGGAGCCGCTAGGGCTCAGGAT Segment# : 5 Offset : 61 1st Codon : 1 G A P R G P H G G A A S A Q D G R C P C G A R R P D S R L L GGCGCTCCCAGAGGCCCTCACGGAGGCGCTGCCTCCGCCCAAGACGGAAGGTGTCCCTGTGGCGCTAGGAGACCCGATAGCAGACTGCTC : LAGE1 Segment# : 6 Offset : 76 1st Codon : 1 G R C P C G A R R P D S R L L Q L H I T M P F S S P M R A E GGCAGATGCCCTTGCGGAGCCAGAAGGCCTGACTCCAGGCTCCTGCAACTGCATATCACAATGCCTTTCTCCAGCCCTATGGAAGCCGAA : LAGE1 Segment# : 7 Offset : 91 1st Codon : 1 Q L H I T M P F S S P M B A B L V R R I L S R D A A P L P R CAGCTCCACATTACCATECCCTTTAGCTCCCCCATGGAGGCTGAGCTCGTGAGAAGGATTCTGTCCAGGGATGCCGCTCCCCTCCCCAGA Gene : LAGE1 Segment# : 8 Offset : 106 1st Codon : 1 LVRRILSRDAAPLPRPGAVLKDPTVSGNLL CTGGTCAGGAGAATCCTCAGCAGAGACGCTGCCCCTCTGCCTAGGCCTGGCGCTGTGCTCAAGGATTTCACAGTGTCCGGCAATCTGCTC Gene : LAGE1 Segment# : 9 Offset : 121 1st Codon : 1 P G A V L K D F T V S G N L L F I R L T A A D H R Q L Q L S  ${\tt CCCGGAGCCGTCCTGAAAGACTTTACCGTCAGCGGAAACCTCCTGTTTATCAGACTGACAGCCGCTGACCATAGGCCAACTGCCAACTGTCC}$ : LAGE1 Gene Segment# : 10 : 136 1st Codon : 1 FIRLTAADHRQLQLSISSCLQQLSLLNWI<sub>T</sub> TTCATTAGGCTCACCGCTGCCGATCACAGACAGCTCCAGCTCAGCATTAGCTCCTGCCTCCAGCAACTGTCCCTGCTCATGTGGATCACA Gene : LAGE1 Segment# : 11 Offset : 151 1st Codon : 1 ISSCLQQLSLL M W I T Q C F L P V F L A Q A P S G Q Gene : LAGE1 Segment# : 12 Offset : 166 1st Codon : 1 QCFLPVFLAQAPSGQRRAA

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CAGTGTTTCCTCCCCGTCTTCCTCGCCCAAGCCCCTAGCGGACAGAGAAGGGCTGCC

Segments in scrambled order:

MAGE-1 #15

A P E E E I W B E L S V M E V Y D G R E H S A Y G E P R K L GCCCCTGAGGAAGAGATTTGGCAAGAGCTCAGCATCATGGAAGTGTATGACGGAAGGGAACACTCCGCCTATGGCGAACCCCAGAAAGCTC

MAGB-1 #4

BEVPTAGSTDPPQSPQGASAFPTTINFTRQGGGGAGGAGTGCCCTACCCACCACCACATCACTCCCCCCAAGGCGCTTTCCCTACCACCACATCAATTTCACAAGGCAA

PRAME #1(

T V W S G N R A S L Y S P P E P B A A Q P M T K K R K V D G ACCOTCTGGCCAATAGGGCTGACCCTTGACCCTGACGCTGACCCAAAAAGAGAAAGGTCGACGGA

MAGE-3 #14

Q I M P K A G L L I I V L A I I A R E G D C A P E E K I W E CAGATTATGCCTAGGCTGGCCTCTGATTATCGTCCTGGCTATCATTGCCAGAGAGGGGGGGAGACTGTGCCCCTGAGGAAAAGATTTGGGAA

PRAME #9

L Q V L D L R K N S H Q D F W T V W S G N R A S L Y S F P B CTGCAAGTGCTCGACCTCAGGAAAAACTCCCACCAAGACTTTTGGACAGTGTGGAGCGGAAACAGAGCCTCCCTGTATAGCTTTCCCGAA

PRAME #8

L D V L L A Q E V R P R R W K L Q V L D L R K N S H Q D F W CTGGATGTGCTCCTGGCTCAGGAAGTGAGACCCAGAAGGTGGAAGTCTCAGGTCCTGAGAAGAAGAATAGCCATCAGGATTTCTGG

NYNSOLD #2

PRAME #24

Q S P S V S Q L S V L S L S G V M L T D V S P E P L Q A L L CAGTCCCCTCCCGTGTCCCGGGGTCTGCTCCCGGGGTCTGCTCCCGGAGCCCTCCAGGCTCTGCTC

MAGE-1 #17

MAGE-1 #6

R Q P S E G S S S R E E E C P S T S C I L E S L F R A V I T AGGCAACCCTCCGAGGGGAAGCCTCCAGCAGAGGGAAGAGGGAAGAGGGACCCTCCACCTCCTGCATTCTGGAAAGCCTCTTCAGAGCCGTCATCACA

BAGE #1

PRAME #34

T P Y D P B P I L C P C F M P N A A ACCITITACGATCCCGAACCCATTCTGTGTCCCTGTTTCATGCCCAATGCCGCT

MAGE-3 #12

I B L M E V D P I G H L Y I F A T C L G L S Y D G L L G D N ATCGAACTGATGGAGGTCGACCCTATCGGACACCTCTACATTTTCGCTACCTGTCTGGGACTGTCCTACGATGGCCTCCTGGGAGACAAT

GAGR-1 #2

RRYVEPPEMIGPMRPEQFSDEVEPATPEG AGGAGATACGTCGAGCCTCCCGAAATGATTGGCCCTATGAGACCCGAACAGTTTAGCGATGAGGTCGAGCCTGCCACACCCGAAGAGGGA

TRP2IN2 #2

EAGGCTGGCGGATTCTTTCCCTGGCTGAAAGTGTATTACTATAGGTTTGTGATTGGCCTCAGGGTCTGGCAATGGGAAGTGATTACTGT

PRAME #1

A A M E R R R L W G S I Q S R Y I S M S V W T S P R R L V B GCCGCTATGGAAAGGAGGCTCCTGGGAAGGCTCCTGGAA

TRP2IN2 #1

A A L M B T H L S S K R Y T B B A G G P P P W L K V Y Y Y R GCCGCTCTGATGGGGCACACCTCAGGTCCAAGGGTACACAGAGGAAGCCGGAGGCTTTTTCCCTTGGCTCAAGGTCTACTATTACAGA

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MAGE-1 #1

A A M S L E Q R S L H C K P E E A L E A Q Q E A L G L V C V GCCGCTATGTCCCTGGAACAGAGAAGCCTCCACTGTAAGCCTGAGGAAGCCCTCGAGGCTCAGCAAGAGGCTCTGGGACTGGTCTGCGTC

Q A A T S S S P L V L G T L B E V P T A G S T D P P Q S P CAGGCTGCCACAAGCTCCAGCTCCCCCCTCGTGCTCGGCACACTCGGAAGAGGTCCCCACAGCCGGAAGCACAGACCCTCCCCAAAGCCCT

PRAME #4

ALELL PRELFPPLFMAAPD GRHSQTLKAM V GCCCTCGAGCTCCTGCCTAGGGAACTGTTTCCCCCCTCTGTTTATGGCTGCCTTTGACGGAAGGCATAGCCAAACCCTCAAGGCTATGGTC

ELSVLEV PEGREDSILG DPKKLLTQHPVQE CAGCTCAGCGTCCTGGAAGTGTTTGAGGGAAGGGAAGACTCCATCCTCGGCGATCCCAAAAAGCTCCTGACACAGCATTTCGTCCAGGAA

ESLQLVPGIDVKEADPTGHSYVLVTCLGLS GAGTCCCTGCAACTGGTCTTCGGAATCGATGTGAAAGAGGGTGACCCTTACCGGACACTCCTACGTCCTCGGTCACCTGTCTGGGACTGTCC

MAGE-3 #5

P D P P Q S P Q G A S S L P T T M N Y P L W S Q S Y E D S S CCCGATCCCCCTCAGTCCCCCCAAGGCGCTAGCTCCCTGCCTACCACAATGAATTACCCTCTGTGGAGCCAAAGCTATGAGGATAGCTCC

A A M Q A R G Q G T G G S T G D A D G P G G P G I P D G P G GCCGCTATGCAAGCCCAAGGCCAAGGCACAGGCGGAAGCACAGAGCACAGAGCACGAGCCCGAACCCGGAACCCGGAACCCGGA

NYNSO1a #12

QCPLPVFLAQPPSGQRRAA 

gp100In4 #2
T W G B G L P S Q P I I H T C V Y P F L P D H L S F G R P F ACCTGGGGCGAAGGCCTCCCCTGCCTATCATTCACACGCGTCTACTTTTTCCTCCCGGATCACCTCAGCTTTGGCAGACCCTTT

S T S C I L B S L P R A V I T K K V A D L V G F L L K Y R AGCACAAGCTGTATCCTCGAGTCCCTGTTTAGGGCTGTGATTACCAAAAAGGTCGCCGATCTGGTCGGCTTTCTGCTCCTGAAATACAGA

A A M Q A E G R G T G G S T G D A D G P G G P G I P D G P G GCCGCTATGCAAGCCGAAGGCAGAGGCACAGGCGGAAGCACAGGCGGATGCCGATGCCGACCCGGACCCGGAATCCCTGACGGACCCGGA

D G P D G Q E M D P P N P B B V K T P B E E M R S H Y V A Q GACGGACCCGATGGCCAAGAGATGGACCCTCCCAATCCCGAAGAGGTCAAGACACCCGGAAGAGGAAATGAGAAGCCATTACGTCGCCCAA

NYNSOla #11

ISSCLQQLSLLMWITQCFLPVFLAQPPSGQ 

ERASATLQ DLV PDECGITDDQ LLALL PSLS GAGAGAGCCTCCGCCACACTGCAAGACCTCGTGTTTGACGAATGCGGAATCACAGACGATCAGCTCCTGGCTCTGCTCCCCTGTCC

MAGB-3 #17

LGDPKKLLTQHPVQENYLBYRQVPGSDPAC 

MAGR-1 #2

B A L E A Q Q E A L G L V C V Q A A T S S S P L V L G T L 

E F Y L A M P F A T P M E A E L A R R S L A Q D A P P L P V GAGTTTTACCTCGCCATGCCCTTTGCCACACCCATGGAGGCTGAGCTCGCCAGAAGGTCCCTGGCTCAGGATGCCCCTCCCCCTCCCCGTC

NYNSO1b #4

B B A P R G V R M A A R L Q G A A GAGGAAGCCCCTAGGGGAGTGAGAATGGCTGCCAGACTGCAAGGCGCTGCC

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BAGE #3

W R L E P E D G T A L C F I F A A TGGAGACTGGAACCGGAACCGGTCTGTGTTTCATTTTCGCTGCC

GAGE-1 #3

E Q P S D E V B P A T P E E G E P A T Q R Q D P A A A Q E G GAGCAATTCTCCGACGAAGTGGAACCCGCTACCCCAGAGGGGAACCCGCTACCCCAAGAGGCAAGACCCTGCCCCAAGAGGGA

MAGE-3 #6

T M N Y P L W S Q S Y E D S S N Q E E E G P S T F P D L E S ACCATGAACTATCCCTCTGGTCCCAGTCCTACGAAGACTCCAGGCAATCAGGAAGAGGCCCTAGCACATTCCCTGACCTCGAGTCC

MAGE-3 #7

N Q E E E G P S T F P D L E S E F Q A A L S R K V A E L V H
AACCAAGAGGGAAGGGGACCCTCCACCTTTCCCGATCTGGAAAGCGGAATTCCAAGCCGCTCTGTCCAGGAAAGTGGCTGAGCTCGTGCAT

PRAME #13

V D L F L K E G A C D E L F S Y L I E K V K R K K N V L R L GTGGATCTGTTTCTGAAAGGAGAAAGGAAAAGGAACTGTTCAGGCTC

NYNSOla #10

TIRLTA A DHRQLQLSISSCLQQLSLLMWIT ACCATTAGGCTCACCAGCCAGCACACTGCCTCAGCACCAGCACACTGCCTCAGCACCAGCACTGCCTCAGCACCAGCACTGCCTCAGCACCAGCACTGCCTCAGCACCAGCACTGCTCCTGCTCAGGATCACA

MAGE-3 #1

A A M P L B Q R S Q H C K P E E G L E A R G E A L G L V G A GCCGCTATGCCTCGGACAGGCGACACCTCTAAGCCTGAGGAAGGCCTCGGGGGAGAGGCTCTGGGACTGGTCGGCGCT

NYNSOla #2

MAGE-3 #19

PRAME #23

I T N C R L S E G D V M H L S Q S P S V S Q L S V L S L S G ATCACAAACTGTAGGCTCAGCGAAGGCGATGTGATGCACCTCAGCCGAA

MAGE-3 #18

NYLBYRQVPGSDPACYBPLWGPRALVBTSY AACTATCTGGAATACAGCAGCTCCCGGAAGCGATCCCGCTTGCTATGAGTTTCTGTGGGGCCCTAGGGCTCTGGTGAGACAAGCTAT

MAGE-3 #11

PRAME #21

Q A L Y V D S L F F L R G R L D Q L L R H V M N P L E T L S CAGGCTCTGTATGTGGATAGCCTCTTTTTTCTGAGAGGCAGACTGGATCAGCTCCTGAGACACTGTCC

PRAME #20

Y I A Q F T S Q F L S L Q C L Q A L Y V D S L F F L R G R L TACATTGCCCAATTCACAAGCCAATTCCTCAGGGGAAGGCTC

PRAME #7

G Q H L H L B T P K A V L D G L D V L L A Q B V R P R R W K
GGCCAACACCTCCACCTCGAGACATTCAAAGCCGTCCTGGATGCCTCGACGTCCTGCCCCAAGAGGTCAGGCCTAGGAGATGGAAA

LAGE1 #10

PRAME #15

C C K K L K I P A M P M Q D I K M I L K M V Q L D S I E D L TGCTGTAAGAACTGAAAATCTTTGCCATGCCCATGCAGGATATCAAAATGATTCTGAAAATGGTCCAGCTCGACTCCATCGAAGACCTC

NYNSO1a #5

GAPRGPHGGAASGLNGCCRCGARGGGACCCGAAAGCAGACTGCTCACGGATGCTGTAGGTGTGGCGCTAGGGGACCCGAAAGCAGACTGCTC

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MAGE-1 #8

KKVADLVG PLLKYRAREPVTKAEMLESVI AAGAAAGTGGCTGACCTCGTGGGATCCCTCAAGTATGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGAGTCCGTGATT

MAGE-1 #13

PRAME #29

S I S A L Q S L L Q H L I G L S N L T H V L Y P V P L B S Y AGCATTAGCGCTCTGCAAAGCCTCATCGGAAAGCTATCCAACCTCACCCATGTGCTCTACCCTGTGCCTCTGGAAAGCTAT

MAGE-3 #19

PRAME #22

D Q L L R H V M N P L E T L S I T N C R L S E G D V M H L S GACCAACTGCTCAGGCATGTGATGCACCTCTGGAAACCCTCAGGCATTACCAATTGCAGACTGTCCGAGGGAGACGTCATGCATCTGTCC

MAGE-1 #19

PRAME #30

S N L T H V L Y P V P L E S Y E D I H G T L H L E R L A Y L AGCANTCTGACACACGTCCTGTGTCCCCCTCGAGTCCTTCGAGAGACCTTCCACCTCGAGAGACCTCCACCTCGAGAGACTGGCTTACCTC

NYNSO1b #1

A A M L M A Q E A L A F L M A Q G A M L A A Q B R R V P R A GCCGCTATGCTCATGGCTCAGGAAGGAGTGCCTAGGGCT

MAGE-1 #10

KNYKHCPPEIFGKASBSLQLVPGIDVKBAD
AAGAATTACAAACACTGTTTCCCTGAGATTTTCGGAAAGGCTAGCGAAAGCCTCCAGCTCGTGTTTGGCATTGACGTCAAGGAAGCCGAT

MAGE-3 #4

TLVBVTLGBVPAABSPDPPQSPQGASSLPT

PRAME #32

HARLRBLLCELGRPSMVWLSANPCPHCGDRCCACGCTAGGCTCAGGCACCCCATCCCCATTGCGGACCCGACCCGACCCCATCCCCCATTGCGGACCAGA

PRAME #25

V M L T D V S P E P L Q A L L E R A S A T L Q D L V F D E C GTGATGCTGAGGGCTAGCCCTCAGGACTCGGTCTTCGATGAGTGT

GAGE-1 #5

E D E G A S A G Q G P K P E A D S Q E Q G H P Q T G C E C B GAGGATGAGGGAGCCTCCGCCGGACAGGGCCAACCCGAAGCCGATGCGAA

MAGE-3 #10

EMLGSVVGNWQYFFPVIPSKASSSLQLVPGGAGATGCTGGGAACTGGCAGTTTTTTTTCCGTCATCTTTAGCAAAGCCTCCAGCTCCTGCAACTGGTCTTTGGA

GAGE-1 #1

A A M S W R G R S T Y R P R P R R Y V E P P E M I G P M R P GCCGCTATGTCCTGGAGGGCGCAGAAGCACATACAGACCCAGACCCAGAAGGTATGTGGAACCCCTGAGATGATCGGACCCATGAGGCCT

PRAME #2

Y I S M S V W T S P R R L V B L A G Q S L L K D E A L A I A
TACATTAGCATGAGCGTCTGGACAAGCCCTAGGAGACTCGTCGAGCACTCCCTGGACAAGGATGAGGCTCTGGCTATCGCT

MAGE-1 #16

LAGE1 #12

Q C P L P V P L A Q A P S G Q R R A A CAGTGTTTCCTCCCCGTCTTCCTCGCCCAAGCCCCTAGCGGACAGAGAGGCCTGCC

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MAGE-3 #20

V K V L H H M V K I S G G P H İ S Y P P L H E W V L R E G E GTGAAAGTGCTCCACCATATGGTCAGGAAGTGCGAGGCGAA

LAGE1 #7

Q L H I T M P P S S P M E A E L V R R I L S R D A A P L P R CAGCTCCACATTACCATCCCCTTAGCTCCCCCATGAGCTCTTAGCTCTTTAGCTCCCCCATGAGAAGGATTCTTCTCCAGGGATGCCGCTCCCCCCAGA

NYNSOla #9

PGVLLKEPTVSGNILTIRLTAAADHRQLQLSCCCGGAGTGCTCCTGAAAGAGTTTACCGTCAGCGGAAACATTCTGACAATCAGACTGACAGCCGCTGACCATAGGCAACTGCAACTGTCC

PRAME #16

KMILKMVQLDSIEDLEVTCTWKLPTLAKPS AAGATGATCCTCAAGATGGTGCAACTGGCATGGATCTGCAAGTGACATGCACATGCAAACTGCCTACCCTCGCCAAATTCTCC

MAGE-1 #14

PLIIVLVMIAMEGGGHAPEEEIWEBLSVMEV

PRAME #17

EVTCTWKLPTLAKFSPYLGQMINLRRLLLSGAGGTCACCTGTACCTCGGAGACTCCCCACACTGGCTAAGTTTAGCCCTTACCTCGGCCAAATGATTAACCTCAGGAGACTGCTCCTGTCC

MAGE-3 #2

EGLEARGEA LGLVGAQAPATEEQEAASCCCTGGCAAGCCCCTGCCACAGAGGAACAGGAAGCCCTAGCTCCAGCTCCAGCCCCAGAGGAACAGGAAGCCCCTAGCTCCAGCTCCAGCTCCAGCCCAGAGGAACAGGAAGCCCCTAGCTCCAGCTCAGCTCCAGCTCCAGCTCCAGCTCCAGCTCAGCTCCAGCTCCAGCTCCAGCTCCAGCTCCAGCTCAGCTCCAGCTCAGCTCCAGCTCAGCTCCAGCTCAGCTCCAGCTCAGCTCCAGCTCAGCTCCAGCTCAGCTCCAGCTCCAGCTCAGCTCAGCTCAGCTCAGCTCAGCTCCAGCTC

MAGE-3 #21

PRAME #19

H I H A S S Y I S P E K E E Q Y I A Q P T S Q P L S L Q C L CACATTCACGCTAGCTCCTACATTAGCCCTGAGAAAGAGGAACAGTATATCGCTCAGTTTACCTCCCAGTTTCTGTCCCTGCAATGCCTC

NYNSOla #3

NYNSOla #4

MAGR-1 #5

NYNSOla #8

PRAME #5

A A P D G R H S Q T L K A M V Q A W P F T C L P L G V L M K GCCGCTTTCGATGCCAGACACTCCAGACACTGAAAGCCATGGTGCAGCCTGGCCCTTTACCTGTCTGCCTCTCGCAGTGCTCATGAAA

MAGE-1 #20

PRAME #27

G I T D D Q L L A L L P S L S H C S Q L T T L S F Y G N S I GGCATTACCGATGACCAACTGCTCCTCCTCCTGCCTAGCCATTGCTCCCAGCTCACCACTGTCCTATTGGCAATAGCATT

GAGE-1 #8

V K T P B B B M R S H Y V A Q T G I L W L L M N N C F L N L GTGAAAACCCCTGAGGAAGAGATGAGTCCCACTATGTGGCTCAGACAGGCATTCTGTGGCTCCTCATGAATAACTGTTTCCTCAACCTC

LAGE1 #11

I S S C L Q Q L S L L M W I T Q C P L P V P L A Q A P S G Q ATCTCCAGCTGTCTGCAACAGCTCAGCCTCCTGGATTACCCAATGCTTTCTGCCTGTGTTTCTGGCTCAGCCTCCCCCCCAA

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PRAME #14

Y L I E K V K R K K N V L R L C C K K L K I F A M P M Q D I TACCTCATCGAAAAGGTCAAGACAAAAAACGTCCTGAGACTGTGTTGCAAAAAGGTCAAGATTTTCGCTATGCCAAGAACATT

MAGE-1 #9

A R E P V T K A E M L E S V I K N Y K H C F P E I F G K A S GCCAGAGAGCCTGGACAAGGCTGGACAAGCCTCCAAAAACTATAAGCATTGCTTTCCCGAAATCTTTGGCAAAGCCTCC

LAGE1 #8

L V R R I L S R D A A P L P R P G A V L K D F T V S G N L L CTGGTCAGGAGATCCTCAGCAGAGACCCTCTCCCTAGCCTAGGCCTTGCCTCAGGATTTCACAGTGTCCGGCAATCTGCTC

PRAME #28

H C S Q L T T L S F Y G N S I S I S A L Q S L L Q H L I G L CACTGTAGCCAACTGACAACCTCAGCTTTTACGGAAACTCCATCTCCATCTCCGCCCTCCAGCTCCCAGCATCTGATTGGCCTC

PRAME #33

M V W L S A N P C P H C G D R T F Y D P E P I L C P C F M P ATGGTCTGGCGCTAACCCTTGCCCTTGCCCTTATGGCGATAGGACATTCTATGACCCTGAGCCTATCCTCTGCCCTTGCTTTATGCCT

gp100In4 #1

A A S W S Q K R S P V Y V W K T W G E G L P S Q P I I H T C GCCCCTAGCTGGAGAGCCCAAAGGAGAGCTTTGTGTATGTGTGGAAGACATGGGGAGAGGGACTGCCTAGCCCAACCCATTATCCATACCTGT

BAGE #2

L L Q A R L M K E E S P V V S W R L E P E D G T A L C P I P CTGCTCCAGGCTCAGGCTCAGGCAGGCCCTCTGCTTTATCTTT .

gp100In4 #3

PRAME #18

MAGE-3 #3

PRAME #6

QAWPPTCLPLGVLMKGQHLHLBTPKAVLDG CAGGCTTGGCCTTTCACATGCCTCCCCCTCGGCGTCCTGATGAAGGGACAGCATCTGCATCTGAAAACCTTTAAGGCTGTGCTCCACGGA

PRAME #12

NYNSO1b #3

A E V P G A Q G Q Q G P R G R E B A P R G V R M A A R L Q G GCCGAAGTGCCTGGGGCTCAGGGACAGCCCTAGGGGAAGGGGAAGAGGCTCCCAGAGGCTCAGGGATGGCCGCTAGGCTCCAGGGA

LACEL #5

G A P R G P H G G A A S A Q D G R C P C G A R R P D S R L L GGCGCTCCCGGGGGGCCCTCCCGCCCCAGACGGGGGGTGTCCCTGTGGCGCTAGGAGACCCGATAGCAGACTGCTC

LACRI BA

G P R G A G A A R A S G P R G G A P R G P H G G A A S A Q D GGCCCTAGGGGAGCCGCTAGGGCTAGGGCTCAGGGTCCCATGGGGAGCCGCTAGGGCTCAGGAT

PRAME #3

GAGE-1 #4

BPATQRQDPAAAQBGGBBBBBAGGAAGGCGAAGGCGTAGCGCTGGCCAAGGCCCTAAGCCTGAGGCTGGGCAAGGCGAAGGCGCAAGGCGCTAGGCCTGAGGCTTGAGGCTTGAGGCTTGAGGCTTAAGCCTTGAGGCT

PRAME #11

PEAAQPMTKKRKVDGLSTEAEQPFIPVEVL

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LAGE1 #6

G R C P C G A R R P D S R L L Q L H I T M P F S S P M E A E GGCAGATGCCTTTGCGGAGCCGAAGGCCTGACTCCAGGCTCTTGCAACTGCATATCACAATGCCTTTCTCCAGGCCTATGGAAGCCGAA

LAGE1 #9

PGAVLKDFTVSGNLLFIRLTAAADHRQLQLSCCCCGGACCGTCCTGACAAGACTTTACCGTCACCGGAAACCTCCTGTTTATCAGACTGACAGCCGTGACCATAGGCAACTGCAACTGCCA

PRAME #31

EDIHGTLHLERLAYLHARLRELLCELGRPS
GAGGATATCCATGCCACACTGCACTGCACACCTCCTCTGTGAGCTCGCCACACCCTCCC

GAGE-1 #6

D S Q B Q G H P Q T G C B C E D G P D G Q B M D P P N P B B GACTCCCAGGAACAGGAACACGCTCTGAGGACAGGATGAGTGTGAGTGTGAGGATGCCCCTGACGGACAGGAAATGGATCCCCCTAACCCTGAGGAA

TRP2IN2 #3

FVIGLRVWQWEVISCKLIKRATTRQPAA

LAGE1 #2

D A D G P G G P G I P D G P G G N A G G P G E A G A T G G R GACGCTGACGGACGCCGGAGGCCCTGGCGTTCCCGATGGCCCTTGGCGGAAACGCTGGCGGACCCGGAGAGGCTGGCGCTTACCGGAGGCAGA

MAGE-1 #12

PTGHSYVLVTCLGLSYDGLLGDNQIMPKTGCCCAAAACCGGACTACCAAATCATGCCCAAAACCGGA

MAGE-3 #9

GAGE-1 #9

T G I L W L L M N N C F L N L S P R K P A A ACCEGAATCCTCTGGCTCCTGATGAACAATTGCTTTCTGAATCTGTCCCCCAGAAAGCCTGCCGCT

MAGE-3 #8

EFQAALSRKVAELVHPLLKYRAREPVTKA

MAGE-1 #18

NYNSOla #6

G C C R C G A R G P E S R L L B P Y L A M P F A T P M E A E GCCTGTTGCAGTCCAGAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAAGCCCGAA

MAGE-3 #13

A T C L G L S Y D G L L G D N Q I M P K A G L L I I V L A I GCCACATGCCTCGGCCTCATGACGACTGCTCGCCGATACCAAATCATGCCCCAAAGCCGGACTGCTCATCATTGTGCTCGCCCATT

LAGE1 #3

G N A G G P G E A G A T G G, R G P R G A G A A R A S G P R G GGCAATGCCGGAGGCCCTGGCGAAGCCGCAGAGGCGCAGAGGCGCAGAGGCGCCTGCCAGAGGCTCCGGCCCTAGGGGA

### Artificial Protein:

APEEBIWEELSVMEVYDGREHSAYGEPRKLEEVPTAGSTDPPQSPQGASAPPTTINPTRQTVWSGNRASLYSPPEPEAAQPWTKKRKVDGQIMPKAGL
LIIVLAIIAREGDCAPEBKIWELQVLDLRKNSHQDPWTVWSGNRASLYSPPELDVLLAQEVRPRRWKLQVLDLRKNSHQDPWQGAMLAAQERRVPRAA
EVPGAQGQQGPRGRQSPSVSQLSVLSLSGVMLTDVSPEPLQALLLTQDLVQBKYLEYRQVPDSDPARYEPLMGPRQPSEGSSSREEGFSTSCILESL
FRAVITAAMAARAVPLALSAQLLQARLMKEESPVSTPYDPEPILCPCFMPNAAIELMEVDPIGHLYIPATCLGLSYDGLLGDNRRYVEPPEMIGPMR
PEQFSDEVEPATPEEGEAGGFPPWLKVYYYRPVIGLRVWQMEVISCAAMERRLMGSIQSRYISMSVWTSPRRLVEAALMETHLSSKRYTEEAGGFPP
WLKVYYYRAAMSLEQRSLHCKPEBALEAQQEALGLVCVQAATSSSSPLVLGTLEEVPTAGSTDPPQSPALELLPRELFPPLFMAAPDGRHSQTLKAMV
ELSVLEVFEGREDSILGDPKKLLTQHFVQEBSLQLVFGIDVKEADPTGHSYVLVTCLGLSPDPPQSPQGASSLPTTMYYPLWSQSYEDSSAAMQAEGQ
GTGGSTGDADGPGGPGIPDGPGQCFLPVFLAQPPSGQRRAATWGEGLPSQPIIHTCVYPFLPDHLSFGRPYSTSCILESLFRAVITKKVADLVGFLLL
KYRAAMQABGRGTGGSTGDADGPGGFGIPDGPGGPBGPBGPBGPBPPBEEVKTPEEBRRSHYVAQISSCLQQLSLLMWITQCFLPVFLAQPPSGQRRASA
TLQDLVFDECGITDDQLLALLPSLSLGDPKKLLTQHFVQENYLEYRQVPGSDPACEALEAQQEALGLVCVQAATSSSSPLVLGTLEFYLAMPFATPMB
AELARRSLAQDAPPLPVEEAPRGYMAARLQGAAMRLEPEDGTALCTIFAAEQFSDEVEPATPEEGEPATQRQDPAAAQBGTMYPLWSQSYEDSSNQ
EEEGGPSTPPDLESNQEEEGFSTFPDLESEPQAALSRKVABLVHVDLFLKEGACDELFSYLIEKVKRKNVLRUTIRLTAADHRQLQLSISSCLQQLSL
LMWITAAMPLEQRSQHCKPEEGLEARGEALGLVGAADASGPGFGIPDGPGGAAGGPGBAGATGGRYEFLWGPRALVETSYVKVLHHVKISGGPHITN
CRLSEGDVMHLSQSPSVSQLSVLSLSGNYLEYRQVFGSDPACYEFLWGPRALVETSYVIFSKASSSLQLVFGIELMEVDPIGHLYIPQALYYDSLPFFL

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 ${\tt RGRLDQLLRHVMNPLETLSYIAQPTSQFLSLQCLQALYVDSLPFLRGRLGQHLHLETPKAVLDGLDVLLAQEVRPRRWKFIRLTAADHRQLQLSISSC$ LQQLSLLMWITCCKKLRIFAMPMQDIKMILKMVQLDSIEDLGAPRGPHGGAASGLNGCCRCGARGPESRLLKKVADLVGFLLLKYRAREPVTKAEMLB SVIYDGLLGDNQIMPKTGFLIIVLVMIAMEGGHSISALQSLLQHLIGLSNLTHVLYPVPLESYIAREGDCAPEBKINEELSVLEVPEGREDSIDQLLR HVMNPLETLSITNCRLSEGDVMHLSRALAETSYVKVLEYVIKVSARVRPPPPSLRSNLTHVLYPVPLESYEDIHGTLHLERLAYLAAMLMAQEALAFL naqgamlaaqerrvpraknykhcppeipgkasesiqivpgidvkeadtivbvtigbvpaabspdppqspqgassiptharireliceigrpsmvwlsa NPCPHCGDRVMLTDVSPEPLQALLERASATLQDLVYDECEDEGASAGQGPKPBADSQEQGHPQTGCECEEMLGSVVGNWQYFFPVIFSKASSSLQLVF GAAMSWRGRSTYRPRPRRYVEPPEMIGPMRPYISMSVWTSPRRLVELAGQSLLKDEALAIAYDGREHSAYGEPRKLLTQDLVQEKYLEYRQQCFLPVP  ${\tt LAQAPSGQRRAAVKVLHHMVKISGGPHISYPPLHEWVLREGEQLHITMPFSSPMEAELVRRILSRDAAPLPRPGVLLKEFTVSGNILTIRLTAADHRQ}$ LQLSKMILKMVQLDSIEDLEVTCTWKLPTLAKPSFLIIVLVMIAMEGGHAPEBEIWEELSVMEVEVTCTWKLPTLAKPSPYLGQMINLRRLLLSEGLE argealglvgaqapateeqeaassssisypplhewvlregeeaahihassyispekeeqyiaqptsqplslqclgnaggpgeagatggrgprgagaar asgpgggprgagaarasgpgggaprgphggaasglnqgasappttinftrqrqpsegsssreeegplarrslaqdapplpvpgvllkeptvsgnilaa fdgrhsqtlkamvqawpptclplgvlmkikvsarvrfffpslrbaalrebeegvaagitddqllallpslshcsqlttlsfygnsivktpebemrshy vaqtgilinlimncplinlissclqqlslimnitqcplpvplaqapsgqyliekvkrkknvlrlcckklkipampmqdiarepvtkaemlesviknykh CPPEIFGKASLVRRILSRDAAPLPRPGAVLKDFTVSGNLLHCSQLTTLSFYGNSISISALQSLLQHLIGLMVWLSANPCPHCGDRTFYDPEPILCPCF mpaaswsqkrsfvyvwktwgeglpsqp1ihtcllqarlmkeespvvswrlepedgtalcp1fvypplpdhlsfgrpfhlnpcdflaapylgqminlrr lllshihassyispekeeqqapateeqeaasssstlvevtigevpaabsqampftclplgvlmkgqhlhletpkavldglsteaeqppipvevlvdlp LKEGACDELPSAEVPGAQGQQGPRGREEAPRGVRMAARLQGGAPRGPHGGAASAQDGRCPCGARRPDSRLLGPRGAGAARASGPRGGAPRGPHGGAAS  ${\tt AQDLAGQSLLKDEALAIAALELLPRELPPPLFMEPATQRQDPAAAQEGEDEGASAGQGPKPEAPEAAQPMTKKRKVDGLSTEAEQPFIPVEVLGRCPC$ CARRPDSRLLQLHITMPFSSPMEAEPGAVLKDFTVSGNLLFIRLTAADHRQLQLSEDIHGTLHLERLAYLHARLRELLCELGRPSDSQEQGHPQTGCE QIMPKTGFLLLKYRAREPVTKAEMLGSVVGNWQYFFPTGILWLLMNNCPLNLSPRKPAAEFQAALSRKVAELVHFLLLKYRAREPVTKAVPDSDPARY eflwgpralaetsyvkvleyvgccrcgargpesrllefylamppatpweaeatclglsydgllgdnqimpkaglliivlaignaggpgeagatggrgp RGAGAARASGPRG

#### Artificial DNA:

GCCCCTGAGGAAGAGATTTGGGAAGAGCTCAGCGTCATGGAAGTGTATGACGGAAGGGAACACTCCGCCTATGGCGAACCCCAGAAAGCTCGAGGAAGT ATAGGGCTAGCCTCTACTCCTTCCCTGAGCCTGAGGCTGCCCAACCCATGACCAAAAAGAGAAAGGTCGACGGACAGATTATGCCTAAGGCTGGCCTC CTGATTATCGTCCTGGCTATCATTGCCAGAGAGGGAGACTGTGCCCCTGAGGAAAAGATTTGGGAACTGCAAGTGCTCGACCTCAGGAAAAACTCCCA CCAAGACTTTTGGACAGTGTGGAGCGGAAACAGAGCCTCCCTGTATAGCTTTCCCGAACTGGATGTGCTCCTGGCTCAGGAAGTGAGACCCAGAAGGT GAGGTCCCGGAGCCCAAGGGCCAACAGGGACCCAGAGGCAGAČAGTCCCCCTCCGTGTCCCAGCTCAGCGTCCTGTCCCTGTCCGGGGTCATGCTCAC CTAGGTATGAGTTTCTGTGGGGCCCTAGGCAACCCTCCGAGGGAAGCTCCAGCAGAGAGGAGGAGGGGACCCTCCACCTCCTGCATTCTGGAAAGCCTC CGTCGTGTCCACCTTTTACGATCCCGAACCCATTCTGTGTCCCTGTTTCATGCCCCAATGCCGCTATCGAACTGATGGAGGTCGACCCTATCGGACACC TCTACATTTTCGCTACCTGTCTGGGGACTGTCCTACGATGGCCTTCCTGGGAGACAATAGGAGATACGTCGAGCCTCCCGAAATGATTGGCCCTATGAGA CCCGAACAGTTTAGCGATGAGGTCGAGGCCTGCCACACCCGAAGAGGGGAGAGGCTGGCGGATTCTTTCCCTGGCTGAAAGTGTATTACTATAGGTTTGT GATTGCCCTCAGGGTCTGGCAATGGGAAGTGATTAGCTGTGCCGCTATGGAAAGGAGAAGGCTCTGGGGAAGCATTCAGTCCAGGTATATCTCCATGT CCGTGTGGACCTCCCCAGAAGGCTCGTGGAAGCCGCTCTGATGGAGACACCTCAGCTCCAAGAGATACACAGAGGAAGCCGGAGGCTTTTTCCCT TGGCTCAAGGTCTACTATTACAGAGCCGCTATGTCCCTGGAACAGAGAGCCTCCACTGTAAGCCTGAGGAAGCCCTCGAGGCTCAGCAAGAGGCTCT GGGACTGGTCTGCGTCCAGGCTGCCACAAGCTCCAGCTCCCCCCTTCGTGCTCGGCACACTGGAAGAGGTCCCCACAGCCGGAAGCACAGACCCTTCCCC AAAGCCCTGCCCTCGAGCTCCTGCCTAGGGAACTGTTTCCCCCCTCTGTTTATGGCTGCCTTTGACGGAAGGCATAGCCAAACCCTCAAGGCTATGGTC GAGCTCAGCGTCCTGGAAGTGTTTGAGGGAAGGGAAGACTCCATCCTCGGCGATCCCAAAAAAGCTCCTGACACAGCATTTCGTCCAGGAAGAGTCCCT GCAACTGGTCTTCGGAATCGATGTGAAAGAGGCTGACCCTACCGGACACTCCTACGTCCTGGTCACCTGTCTGGGACTGTCCCCCGATCCCCCTCAGT CCCCCAAGGCGCTAGCTCCCTGCCTACCACAATGAATTACCCTCTGTGGAGCCCAAGCCTATGAGGATAGCTCCGCCGCTATGCAAGCCCAAGGCCAA GECACAGECGGAAGCACAGECGATGCCCCTGGCGGACCCGGAATCCCTGACGGACAGTGTTTCCTCCCGTCTTCCTCGCCCAACC CCCTAGCGGACAGAGAAGGGCTGCCACCTGGGGCGAAGGCCTCCCCTCCCAGCCTATCATTCACACATGCGTCTACTTTTTCCTCCCGGATCACCTCA GCTTTGGCAGACCCTTTAGCACAAGCTGTATCCTCGAGTCCCTGTTTAGGGCTGTGATTACCAAAAAAGGTCGCCGATCTGGTCGGCTTTCTGCTCCTG AAATACAGAGCCGCTATGCAAGCCGAAGGCAGAGGCACAGGCGGAAGCACAGGCGATGCCCTGGCGGACCCGGAATCCCTGACGGACCCGG AGACGGACCCGATGGCCAAGAGATGGACCCTCCCAATCCCGAAGAGGTCAAGACACCCGAAGAGGGAAATGAGAAGCCATTACGTCGCCCAAATCTCCA ACACTGCAAGACCTCGTGTTTGACGAATGCGGAATCAGACGATCAGGTCCTGGCTCCCTGCCTCCCTGCCGAGAACCCCTAAGAAACTGCT CACCCAACACTTTGTGCAAGAGAATTACCTCGAGTATAGGCAAGTGCCTGGCTCCGACCCTGCGTGAGGCTCTGGAAGCCCAACAGGAAGCCCTCG GCCTCGTGTGTGCAAGCCGCTACCTCCAGCTCCAGCCCTCTGGGTCCTGGGGAACCCTTCGAGTTTTACCTCGCCATGCCCTTTGCCACACCCATGGAG GCTGAGCTCGCCAGAAGGTCCCTGGCTCAGGATGCCCCCTCCCCTCCCGTGGAGGAAGCCCCTAGGGGAGTGAGAATGGCTGCCAGACTGCAAGGGGG TGCCTGGAGACTGGAACCCGGAAGACGGAACCGCTCTGTGTTTCATTTTCGCTGCCGAGCAATTCTCCGACGAAGTGGAACCCCGCTACCCCTGAGGAAG GCGAACCCGCTACCCAAAGGCAAGACCCTGCCGCTGCCCAAGAGGGGAACCATGAACTATCCCCTCTGGTCCCAGTCCTACGAAGACTCCAGCAATCAG TCTGTCCAGGAAAGTGGCTGGGCTCGTGCATGTGGATCTGTTTCTGAAAGAGGGGAGCCTGTGACGAACTGTTTAGCTATCTGATTGAGAAAGTGAAAA GGAAAAAGAATGTGCTCAGGCTCACCATTAGGCTCACCGGTGCCGATCACAGCAGCAGCTCCAGCATTAGCTCCTGCCTCCAGCAACTGTCCCTG CTCATGTGGATCACAGCCGCTATGCCTCTGGAACAGAGAAGCCAACACTGTAAGCCTGAGGAAGGCCTCGAGGCTAGGGGAGAGGCCTCTGGGACTGGT CGGCGCTGACGCTGACGGACCCGGAGGCCCTGGCATTCCCGATGGCCCTGGCGGAAACGCTGGCGGACACGCTGGCGGTACCGGAGGCAGAT TGTAGGCTCAGCGAAGGCGATGTGATGCACCTCAGCCAAAGCCCTAGCGTCAGCCAACTGTCCGTCAGCCTCAGCGCAAACTATCTGGAATACAG ACAGGTCCCCGGAAGCGATCCCGCTTGCTATGAGTTTCTGTGGGGCCCCTAGGGCTCGGTCGAGACAAGCTATGTGATTTTCTCCAAGGCTAGCTCCA AGAGGCAGACTGGATCAGCTCCTGAGACACGTCATGAATCCCCTCGAGACACTGTCCTACATTGCCCAATTCACAAGCCAATTCCTCAGCCTCCAGTG TCTGCAAGCCCTCTACGTCGACTCCCTGTTTTTCCTCAGGGGAAGGCTCGGCCAACACCTCCACCTCGAGACATTCAAAGCCGTCCTGGATGGCCTCG CTCCAGCAACTGTCCCTGCTCATGTGGATCACATGCTGTAAGAAACTGAAAATCTTTGCCATGCCCATGCAGGATATCAAAATGATTCTGAAAATGGT

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CCGAAAGCAGACTGCTCAAGAAAGTGGCTGACCTCGTGGGATTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGAAATGCTCGAG TAGCATTAGCGCTCTGCAAAGCCTCCTGCAACACCTCATCGGACTGTCCCAACCTCACCCATGTGCTCTACCCTGTGCCTCTGGAAAGCTATATCGCTA GGGAAGGCGATTGCGCTCCCGAAGAGAAAATCTGGGAGGAACTGTCCGTGCTCGAGGTCTTCGAAGGCAGAGAGGATAGCATTGACCAACTGCTCAGG CATGTGATGAACCCTCTGGAAACCCTCAGCATTACCAATTGCAGACTGTCCGAGGGGAGACGTCATCTGTCCAGGGCTCTGGCTGAGACAAGCTA ATGGCCCAAGGCGCTATGCTCGCCGCTCAGGAAAGGAGTGCCTAGGGCTAAGAATTACAAACACTGTTTCCCTGAGATTTTCGGAAAGGCTAGCGA AAGCCTCCAGCTCGTGTTTGGCATTGACGTCAAGGAAGCCGATACCCTCGTGGAAGTGACACTGGGAGAGGTCCCCGCTGCCGGAAAGCCCTGACCCTC CCCAAAGCCCTCAGGGAGCCTCCAGCCTCCCCACACACGCTAGGCTCAGGGAACTGCTCTGCGAACTGGGAAGGCCTAGCATGGTGTGGCTGTCCGCC AATCCCTGTCCCATTGCGGAGACAGAGAGAGTGATGCTGACAGCCTCAGCCCTCCAGCATGCGAAAAGGGCTACGCTACCCTCCAGA TCTGGTCTTCGATGAGGAGGAGGAGGAGGAGCCTCCGCCGGACAGGGCCCAAACCCGAAGAGCCAATGCCAAGAGCCAAGCCCAAACCGGAT GCGANTGCGANGAGATGCTGGGANGCGTCGTGGGANACTGGCAGTATTTCTTTCCCGTCATCTTTAGCANAGCCTCCAGCTCCCTGCANCTGGTCTTC GGAGCCGCTATGTCCTGGAGAGGCAGAAGCACATACAGACCCAGACCCAGAAGGTATGTGGAACCCCCTGAGATGATCGGACCCCATGAGGCCTTACAT TAGCATGAGCGTCTGGACAAGCCCTAGGAGACTGGTCGAGCTCGCCGGACAGTCCCTGCTCAAGGATGAGGCTCTGGCTATCGCTTACGATGGCAGAG AGCATAGCGCTTACGGAGAGCCTAGGAAACTGCTCACCCAAGACCTCGTGCAAGAGAAATACCTCGAGTATAGGCAACAGTGTTTCCTCCCCGTCTTC CTCGCCCAAGCCCCTAGCGGACAGAGAAGGGCTGCCGTGAAAGTGCTCCACCATATGGTCAAGATTAGCGGAGGCCCTCACATTAGCTATCCCCCTCT GCATGAGTGGGTGCTCAGGGAAGGCGAACAGCTCCACATTACCATGCCCCTTTAGCTCCCCCATGGAGGGCTCGTGAGAAGGATTCTGTCCAGGG ATGCCGCTCCCCTCCCCAGACCCGGAGTGCTCCTGAAAGAGTTTACCGTCAGCGGAAACATTCTGACAATCAGACTGACAGCCGCTGACCATAGGCAA  $\tt CTCCTTCCTCATCATTGTGCTCGTGATGGATGGCTGGAGGGGACACGCTCCCGAAGAGGGAAATCTGGGAGGAACTGTCCGTGATGGAGGTCGAGG$ TCACCTGTACCTGGAAGCTCCCCACACTGGCTAAGTTTAGCCCTTACCTCGGCCAAATGATTAACCTCAGGAGACTGCTCCTGTCCGAGGGGACTGGAA GCCAGAGGCGAAGCCCTCGGCCTCGTGGGAGCCCAAGCCCCTGCCACAGAGGGAACAGGAAGCCGCTAGCTCCAGCTCCATCTCCTACCCTCCCACCTCCA CGAATGGGTCCTGAGAGAGGGAGAGGAGGCACCTCACATTCACGCTAGCTCCTACATTAGCCCTGAGAAAAGAGGGAACAGTATATCGCTCAGTTTACCT CCCAGTTTCTGTCCCTGCAATGCCTCGGCAATGCCGGAGGCCCTGGCGAAGCCGGAGCCCACAGGGGGAAGCGGACCCAGAGGCGCTGGCGTGCCAGA GCCTCCGGCCCTGGCGCAGGCCCTAGGGGGAGCCGGAGCCGCTAGGGGTAGCGGACCCGGAGGCGGGGGCCCCTAGGGGGACCCCATGGCGGAGCCGCTAG TTCGATGGCAGACACTCCCAGACACTGAAAGCCATGGTGCAAGCCTGGCCCTTTACCTGTCTGCCTCTGGGAGTGCTCATGAAAATCAAAGTGTCCGC CAGAGTGAGATTCTTTTTCCCTAGCCTCAGGGAAGCCGCTCTGAGGAGGGGAAGGCGTACGCCGCTGGCATTACCGATGACCAACTGCTCGCCCC TCCTGCCTAGCCTCAGCCATTGCTCCCAGGTCACCACTGTCCTTCTATGGCAATAGCATTGTGAAAACCCCTGAGGAAGAGATGAGGTCCCACTAT GTGGCTCAGACAGGCATTCTGTGGCTGCTCATGAATAACTGTTTCCTCAACCTCATCTCCAGCTGTCTGCAACAGCTCAGCCTCCTGATGTGGATTAC AAAAGCTCAAGATTTTCGCTATGCCTATGCCAAGACATTGCCAGAGAGCCTGTGACAAAGGCTGAGATGCTGGAAAGCGTCATCAAAAACTATAAGCAT TGCTTTCCCGAAATCTTTGGCAAAGCCTCCCTGGTCAGGAGAATCCTCAGCAGAGACGCTGCCCCTCTGCCTAGGCCTTGCCTCAAGGATTT CACAGTGTCCGGCAATCTGCTCCACTGTAGCCAACTGACAACCCTCAGCTTTTACGGAAACTCCATCTCCATCTCCGCCCTCCAGTCCCTGCTCCAGC ATCTGATTGGCCTCATGGTCTGGCTCAGCGCTAACCCTTGCCCTCACTGTGGCGATAGGACATTCTATGACCCTGAGCCTATCCTCTGCCCTTGCTTT ATGCCTGCCGCTAGCTGGAGCCAAAAGAGAAGCTTTGTGTATGTGTGGAAGACATGGGGGAGAGGGACTGCCTAGCCCAACCCATTATCCCATACCTGTCT TTCTGCCTGACCATCTGTCCTTCGGAAGGCCTTTCCATCTGAATTTCTGTGACTTTCTGGCTGCCCCCTATCTGGGACAGATGATCAATCTGAGAAGG CTCCTGCTCAGCCATATCCATGCCTCCAGCTATATCTCCCCCGAAAAGGAAGAGCAACAGGCTCCCGCTACCGAAGAGCAAGAGGCTGCCTCCAGCTC AGCATCTGCATCTGGAAACCTTTAAGGCTGTGCTCGACGGACTGTCCACCGAAGCCGAACAGCCTTTCATTCCCGTCGAGGTCCTGGTCGACCTCTTC CTCAAGGAAGGCGCTTGCGATGAGCTCTTCTCCGCCGAAGTGCCTGGCGCTCAGGGGACAGGCCAAGGCCCTAGGGGAAGGGAAGAGGCTCCCAGAGGCGT CAGGATGGCCGCTAGGCTCCCAGGGGGCCCTCCCGGGAGGCCCTCCCCCCAAGACGGAAGGTGTCCCTGTGGCGCTAGGAGAC GGAGCCTGCCACAGAGACAGGATCCCGCTGCCGCTCAGGAAGGCGAAGACGAGACGCTAGCGCTAGGCCCAAGGCCCTAAGCCTGAGGCTCCCGAAG CCGCTCAGCCTATGACAAAGAAAGGAAAGTGGATGGCCTCAGCACAGAGGCTGAGCAACCCTTTATCCCTGTGGAAGTGCTCGGCAGATGCCCTTGC GGAGCCAGAAGGCCTGACTCCAGGCTCCTGCAACTGCATATCACAATGCCTTTTCTCCAGCCCTATGGAAGCCCGAACCCGGAGCCGTCCTGAAAGACTT TACCGTCAGCGGAAACCTCCTGTTTATCAGACTGACAGCCGCTGACCATAGGCAACTGCAACTGCCAGGGATATCCATGCCACACTGCCACTGGGAAA GGCTCGCCTATCTGCATGCCAGACTGAGAGAGCTCCTGTGTGAGCTCGGCAGACCCCTCCGACTCCCAGGAACAGGGACACCCTCAGACAGGCTTGTGAG TETGAGGATGGCCCTGACGGACAGGAAATGGATCCCCCTAACCCTGAGGAATTCGTCATCGGACTGAGAGTGTGGCAGTGGGAGGTCATCTCCTGCAA ACTGATTAAGAGAGCCACAACCAGACAGCTGCCGCTGACGCTGACGGACCCGGAGGCCCTGGCATTCCCGATGGCCCTGGCGGAAACGCTGGCGGAC CCGGAGAGGCTGCCGCTACCGGAGGCAGACCCACAGGCCATAGCTATGTGCTCGTGACATGCCTCGGCCTATGACTATGACGGACTGCTCGGCCATAAC CAAATCATGCCCAAAACCGGATTCCTCCTGCTCAAGTATAGGGCTAGGGAACCCGTCACCAAAGCCGGAAATGCTCGGCTCGGCCAATTGGCA ATACTTTTTCCCTACCGGAATCCTCTGGCTCCTGATGAACAATTGCTTTCTGAATCTGTCCCCCAGAAAGCCTGCCGTGAGTTTCAGGCTGCCCTCA GCAGAAAGGTCGCCGAACTGGTCCACTTTCTGCTCCTGAAATACAGAGGCCAGAGAGCCTGTGACAAAGGCTGTGCCTGACCCTGCCAGATAC GAATTCCTCTGGGGACCCCAGAGCCCTCGCCGAAACCTCCTACGTCAAGGTCCTGGAATACGTCGGCTGTTGCAGATGCGGAGCCCAGAGGCCCTGAGTC CAGGCTCCTGGAATTCTATCTGGCTATGCCTTTCGCTACCCCTATGGAAGCCGAAGCCCACATGCCTCGGCCTATGACGGACTGCTCGGCCGATA ACCAAATCATGCCCAAAGCCGGACTGCTCATCATTGTGCTCGCCATTGGCAATGCCGGAGGCCCTGGCGAAGCCGGAGCCCACAGGCGGAAGGGGACCC AGAGGCGCTGGCGCCCAGAGCCTCCGGCCCTAGGGGA

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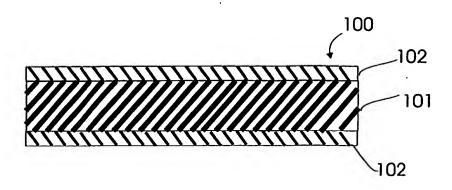


FIGURE 28

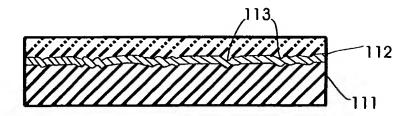


FIGURE 29

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# Cassettes for construction of a full-length HIV Savine

### Cassette Al

ggatccaccATGACAGGCCCTTGCACAAACGTCAGCACCGTGCAATGCACACGGAATCAGACCCGTCGTGTCCA CCCAACTGCTCCTGAATGGCTCCCTGAGAAGCCTCTACAATACCGTCGCCACACTGTGGTGCGTCCACCAAAGGAT TGACGTCAGGGACACAAAGGAAGCCCTCGACAAAATCGAACTCGGCGATGGCGGAGGCGCTGAAAGGCAAGGCACC TCCAGCTCCTTCAACTTTCCACAAATCACTGTGGCAAAGGCCTCTGGTCACCGAACCCTTCAGAAAAAAGAATC  ${\tt CCGATATGGTGATTTACCAGTACATGGACGATCTGTATGTGGGAAGCGATCTGGAAATCGGACAGCATTTTACCAC}$ ACCCGATAAGAAACACCAAAAGGAACCACCATTCCTCTGGATGGGATACGAACTGCATCCCGATAGGTGGACCGTC CAGCCTCTTAATTTCCCTCAGATTACCCTCTGGCAGCGTCCCCTCGTGACAATCAAAATCGGCGGACAGCTCATAG AGGCTCTGCTCGACACGGCTCCTATGGCAGAAAGAAACGTAGGCAACGTAGACGCGCTCCTCAGAGCAGCAAGGA TCACCAATACCCTATCTCTGAGCAACCCCTCTCCTTCTTTAGGGAAAACCTGGCTTTCCAGCAAGGTAAAGCCAGA GAGTTTTCCAGCGAACAGACAAGAGCCAATAGCTCCGCCTCCAGGAAGAGCCCCCAAATCTCCGGCGAAAGCTCCG TCATTCTGGGATCTGGCACCAAAAACGCCGCTACTAGAAGAATCGAAGTGAAAGATACCAAAGAGGCTTTGGATAA GATTGAGGAGGTGCAAAAGAAAAGCGAGCAAAAAGACACAACAGGCTGCCGCTAAAGCCGGATACGTCACCGATAGG GGAAGGCAAAAGATTATCTCCCTGACAGAGACAACCAATCAGAAAACCGAACTGCATGCCATTCAAGAAGCCACTA CCACACTGTTTTGCGCCAGCGATGCCAAAGCCTATGAGACAGAGGTCCACAATGTGTGGGCCACACACGCTTGCGT CCCCGCTGACGATACAGTGCTGGAGGAGATGAACCTCCCCGGAAAATGGAAGCCTAAGATGATTGGCGGAATCGGC GGATTCATTAAGGTGAGAAAAATCGGACCCGAAAACCCTTACAATACCCCAATCTTCGCTATCAAGAAAAAGGACT CCACCAAATGGAGAAAGCTCGTGGATTTCAGAGTTAGGATTATCAATATCCTCTACCAAAGCAATCCCTATCCTAG CTCCGAAGGCTCCAGGCAAACCAGAAAGAATAGGAGAAGGAGATGGGGAGGCGAACGGGGTAGGGATAGGTCCGTG AGACTGGTCAACGGATTCTTAGCCCTCGCCTGGGACGATCTGAGAAACCTCTGCCTCTTCGAAAACCTCTGGGTCA CCGTCTACTATGGCGTCCCCGTCTGGAGAGAGGCTGCCACAACCCTCTTCTGTGCCTCCGACGCTAAGGCTTACGC TGCCATGGCTGGCAGAAGCGGCGCACAGACGAAGAGCTCCTGAGGGCTATCAGAATCATTAACATTCTGTATCAG TCCAACCCTTACCCTTCCGCTAGTATGAGAATCAGAACCTGGAACAGCCTGGTCAAGCATCACATGCACATCTCCA AGAAAGCCAAAGGCTGGTTCTATAGGCATCACTTTGAGGAGTCCGAGCTCGTGAATCAGATTATCGAAAAGCTCAT CAAAAAGGAAAAGGTCTACCTATCATGGGTACCAGCCCACAAGGGAATCGGACAAACCAAAGAGCTCCAGAAACAG ATTATCAAAATCCAAAACTTTAGGGTCTACTATAGGGATAGCAGAGACCCTATCTGGAAGGGACCCAAAAGCTTTG TCTGAAACCCGAACCCACAGCCCCTCCCGCTGAGAATTTCAGATTCGGTGAGGAAACTACACCCTCCCAAAAGCAA: GAGCAAAAGGATAAGGAGCAATACGATCAGATTCTTATTGAGATTTGCGGCAAGAAAGCTATTGGTACGGTGCTCG TGGGACCTACCCCTGTGAATATCATTGGCAGAATTTACGAAACCTATGGCGATACCTGGGAGGGCGTCGAGGCTCT GATCAGAATCCTCCAGCAACTGATGTTTATCCATTTCAGAATCGGATGTTTTCATTGCCAAGTGTGTTTTCTCACC AAAGGTCTCGGCATTAGCCACGGAAGGAAAAAGAGAAAACAGAGAGGGGAGCTCCCCAAGCTGCCATGGACCCCG TGGACCCCAAGCTGGAGCCTTGGAAACACCCTGGCTCCCAGCCTAAGACAGCCTGTTACAAATGCTATTGCAAAAA CTCAAGTCCCTGTTTGGCAATGACAATTTCAATATGTGGAAGAATGACATGGTGGAACAGATGCAAGAAGACATTA TCTTACTATGGGACCAAAGCCTCAAGCCTTGCGTCAAGCTCGACGTCGGCGATGCCTATTTCTCCGTGCCTCTGGA GGCCAAGTGAATTGCTCACCAGGCATTTGGCAACTGGATTGCACACCCTGGAGGGAAAGATTATCCCTAAGGTCA TAGCATGGATGACCTCTACGTCGGCTCCGACCTGG

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AGATTGGCCAACATAGGACCAAAATCGAAGAGCTCAGGGAACACCTCCTGAAATGGGGACTCACCGAAACCACAAA CAGACAATGGCAGGACAAAGATTGAGGAACTGAGACCGCATCTGCTCAAAATGGGGCTTCACAACCCCTGACAAAAA AAGAGACGCAGAGAAAATCACACAATGAATGGCCATACTGCCACAGAGTCCCAGAATCAGCAAGACAGAAACGAAA AGGAACTGCTGGAGCTCGACAAATGGGCAAGCCTCTGGAATTGGTTTAACATTACCGACACCCGGAAATAGCTCCAA AGTGTCCCAGAATTACCCTATCGTCCAGAATGTCCAAGGCCAAATGGTCCACCAACCCCTCTCCCCCAGACTCATC GGACTGAGAATCGTTTTCGCTGTGCTCAGCATTATCAATAGGGTCAGGCAAGGCTATAGCCCTCTGTCCTTCCAAA CCCTCCCCTCATCCATCTGCAATACTTTGACTGTTTCGCTGACTCCACCATTAGGAGAGCCATCTTGGGACACAT AGTGAGAAGGAGATGCGAATACGCTGTGGGACTCGGAGCCATGTTCCTTGGCTTCTGGGTGCCGCTGGCTCCACC ATGGGCGCTGCCTCCATGACACTGACAGTGCAAGCCTATGACCCTAGCAAAGACCTCATTGCTGAGATTCAGAAAC AGGGCCAGGGTCAGTGGACATTTCAGATTTTCCAAGAGCCTTTCAAAAACGGAACCGTCCTGGTCGGCCCTACACC CGTCAACATCATCGGAAGGAACATGCTGACACAGCTTGGCCGCACTCTCAACTTTCCCATTAGCAAAGGCAGCCCT GCTATCTTTCAGTCCAGCATGCCACAGATTCTGGAGCCTTTTAGGATAAAAAACCCTGAGATGGTCATCTATCAGT ATCCTAGCCCTCTGACATTCGGATGGTGTTTCAAACTGGTCCCCGTGGACCCCAGCGAAGTGGAAGAGATCAACAA GGGCGAAAACAATTGCCCCCTGTTTAGGAAATACACAGCCTTTACCATTCCCTCCATCAATAACGAAACCCCTGGC ATTAGGTATCAGTATAACGTCCTGCCTCAGGGATGGGGAAGCACAATGGGAGCCGCCAGCATGACCCTCACCGTCC AGGCTAGGCTACTGCTCAGCGGAATCGTCCAGCAACAGAGCAATCTGCTGGAGGAGAATAGGGAAATCCTCAGAGA GCCTGTGCATGGCGTCTACTACGATCCCTCCAAGGATCTGGTCGCTGAAAATCCAAAAGCAAGGCAGAGAGGAACTG TCCACCATGGTGGATATGGGAAACTACGACCTCGGAGTGGACAATAACCTCGCCGCTATTAGAATCCTGCAACAGC TCATGTTCATTCACTTTAGGATTGGCTGCCAGCACTCCAGGATTGGCATCATCCGTCAGAGAAGGGCCAGAGCTCC CAGGAAAAAGGGATGCTGGAAGTGTGGCAGAGAGGGGACACCAGATGAAGGATTGCACTGAGAGACAGGCTAACTTT ATGGCGTCAGCATTGAGTGGAGGATAAGGGAAAGGGCTGAGGATAGCGGCAACGAAAGCGAAGGCGACACAGAAGA GCTCAGCACATTGGTGGACATGGGCAATTACGATCTGTCTAGCCCTGCCCCCAGGGGACCCGATAGGCTGGAGAGA ATCGAAGAGGAAGCCGAGAGCAAGGCAGAGGCAGAAGCGTCAGGCTCGTGAATGGCAGAGAGGTCGAGGAAGTCA GTGGCCAGCTTCTCTCCGAGCAAACAGGGGCTAACTCCTCTACAAGCAGAAAGCTGGGAGACGGAGGCGGAGCCG ACAGACAGGGAACAAGCTCCAGCTGTTTCAATTGCGGCAAAGAGGGGACACATTGCCAAAAAACTGTAGGGCCCCTCG CAAGAAAGGTTGTTGGAAATGCGGAAAGGAAGGCCATCAAATGAAAGACTGTACCGAAAGGCAAGCCAATTTCCTC GGCAAAATCTGGCCCTCCAACAAAGGCAGACCCGGAAACTTTCTCCAAAGCAAATGGCTCTGGTATATCAAAATCT TTATCATGATCGTCGGTGGACTGATTGGCCTCAGGATTATCTTTGCCGTCCTGTCCATCGTTAACGGAGCCGTGAG CCGAGACCTCGATAAACATGGCGCTATTACAAGCTCCAATACCGCTGACATAACGCTGACTGTCTGGCTGAAG GCTGCTGCCATGACACCCCTGGAGATCATCGCTATCGTCGCCTTTATCGTCGCCCTCATCATAGCCATTGTGGTCT GGACAATCGTCTACATTGAGTATGTCGACtgaagatctgaattc

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### A2 fragment

ggatccaccATGACAGGCCCTTGCACAAACGTCAGCTCCGTGCAATGCACACAGAATCAAACCCGTCGTGTCCAA CCCAACTGCTCCTGAATGGCTCCCTGAAAAGCCTCTACAATACCGTCGCCACACTGTGGTGTGTCCACCAAAGGAT TGAGGTCAAGGACACAAAGGAAGCCCTCGACAAAATCGAACTCGGCGATGGCGGAGGCGCTGAAAGGCAAGGCACC TCCAGCTCCATCAACTTTCCACAAATCACACTGTGGCAAAGGCCTCTGGTCACCGAACCCTTCAGAAAAGAGAATC CCGAAATGGTGATTTACCAGTACATGGACGATCTGTATGTGGGAAGCGATCTGGAAATCGGACAGCATTTTACCAC ACCCGATAAGAAACACCAAAAGGAACCACCATTCCTCTGGATGGGATACGAACTGCATCCCGATAGGTGGACCGTC CAGCCTTTTAATTTCCCTCAGATTACCCTCTGGCAGCGTCCCCTCGTGACAATCAAAATCGGCGGACAGCTCATAG AGGCTCTGCTCGACACAGGCTCCTATGGCAGAAAGAAACGTAGGCAACGTAGACGCGCTCCTCAGAGCAGAAAGGA TCACCAATACCCTATCTCTGAGCAACCCCTCTCCTTCTTTAGGGAAAACCTGGCTTTCCAGCAAGGTAAAGCCAGA GAGTTTTCCAGCGAACAGACAGGAGCCAATAGCTCCGCCTCCAGGAAGAGCCCCCAAATCTCCGGCGAAAGCTCCG TCATTCTGGGATCTGGCACCAAAAACGCCGCTACTAGAAGAATCGATGTGAGAGATACCAAAGAGGCTCTGGATAA GATTGAGGAGGAGCAAAACAAAAGCAAGCAAAAGACACAACAGGCTGCCGCTAAAGCCGGATACGTCACCGATAGG GGAAGGCAAAAGATTATCTCCCTGACAGAGACAACCAATCAGAAAAACCGAACTGCCATGCCATTCAAGAAGCCGATA CCACACTGTTTTGCGCCAGCGATGCCAAAGCCTATGACACAGGGTCCACAATGTGTGGGCCACACACGCTTGCGT CCCCGCTGACGATACAGTGCTGGAGGAGATGAACCTCCCCGGAAAATGGAAGCCTAAGATGATTGGCGGAATCGGC GGATTCATTAAGGTGAGAAAGATCGGACCCGAAAACCCTTACAATACCCCAATCTTCGCTATCAAGAAAAAGAACT CCACCAAATGGAGAAAGCTCGTGGATTTCAGAATTAGGATTATCAAAATCCTCTACCAAAGCAATCCCTATCCTAG CTCCGAAGGCACCAGGCAAACCAGAAAGAATAGGAGAAGGGGGATGGGGAGGCGAACAGGGTAGGGATAGGTCCGTG AGACTGGTCAACGGATTCTTAGCCCTCGCCTGGGACGATCTGAGAAGCCTCTGCCTCTTCGACAACCTCTGGGTCA CCGTCTACTATGGCGTCCCCGTCTGGAGAGAGGCTAACACCCTCTTCTGTGCCTCCGACGCTAAGGCTTACGC TGCCATGGCTGGCAGCAGCGCACACAGACGAAGAGCTCCTGAAGGCTGTCAGAATCATTAAGATTCTGTATCAG TCCAACCCTTACCCTTCCGCTAGTATGAAAATCAGAACCTGGAAGAGCCTGGTCAAGCATCACATGTACATCTCCA AGAAAGCCAATGGCTGGTTCTATAGGCATCACTTTGAGGAGTCCGAGGTCGTGAATCAGATTATCGAAAAGCTTAT CAAAAAGGAAAAGGTCTACCTATCATGGGTACCAGCCCACAAGGGAATCGGACGAACCAAAGAGCTCCAGAAACAG ATTATCAAAATCCAAAACTTTAGGGTCTACTATAGGGATAGCAGAGACCCTATCTGGAAGGGACCCAAAAGCCTTG TCTGAGACCCGAACCCACAGCCCCTCCCGCTGAGAATTTCGGATTCGGTGAGGAAACTACACCCTCCCAAAAGCAA GAGCCAAAGGATAAGGAGCAATACGATCAGATTATTATTGAGATTTGCGGCAAGAAAGCTATTGGTACAGTGCTCG TGGGACCTACCCCTGTGAATATCATTGGCAGAATTTACGAAACCTATGGCGATACCTGGGAGGGCGTCGAGGCTCT GATCAGAATCCTCCAGCAACTGATGTTTATCCATTTCAGAATCGGATGTTTTCATTGCCAAGTGTGTTTTCTCACC AAAGGTCTCGGCATTAGCCACGGAAGGAAAAAGAGAAAACAGAGAAGGCGAGCTCCCCAAGCTGCCATGGACCCCG TGGACCCCAACCTGGAGCCTTGGAAACACCCTGGCTCCCAGCCTAAGACGCCTGTAACAAATGCTATTGCAAAAA GTGCCCTAGCGAAGAGACACCCCTAGCCAGAAACAGGAACAGAAGAACAAAGACTCTACCCCCCTTTAGCCAGC CTCAAGTCCCTGTTTGGCAATGACAATTTCAATATGTGGAAGAATAACATGGTGGAACAGATGCAAGAAGACATTA TCTCACTATGGGACCAAAGCCTCAAGCCTTGCGTCAAGCTCGACGTCGGCGATGCCTATTTCTCCGTGCCTCTGGA GGCCAAGTGAATTGCTCACCAGGCATTTGGCAACTGGATTGCACACCTGGAGGGAAAGATTATCCCTAAGGTCA TAGCATGGATGACCTCTACGTCGGCTCCGACCTGGAGATTGGCCAACATAGGACCAAAATCGAAGAGCTCAGGGCA

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CACCTCCTGAGATGGGGACTCACCGACACCACAAACCAAAAGACTGAGCTCCACGCTATCCATCTGGCTCTGCAAG ACTCCGGCTTAGAGGTCAACATTGTGACAGACATTCCCGCTGAGACTGGTCAAGAGACCACCTATTTCATTCTGAA ACTGGCTGGCAGATGGCCTGTGAGAATCATTCACACAGACAATGGCAGGACAAAGATTGAGGAACTGAGACCGCAT CTGCTCAAATGGGGCTTCACAACCCCTGACAAAAAGCGTCAGAAAGAGCCTCCCTTTCTGTCTAGTGTCAAGAAAC CACAGAGTCCCAGAATCAGCAAGACAGAAACGAAAAGGAACTGCTGGAGCTCGACAAATGGGCAAGCCTCTGGAAT TGGTTTAACATTACCGACACCGGAAGTAGCTCCCAAGTGTCCCAGAATTACCCTATCGTCCAGAATCTCCAAGGCC AAATGGTCCACCAACCCATCTCCCCCAGACTCGTCGGACTGAGAATCATTTTCGCTGTGCTCAGCATTATCAATAG GACTCCACCATTAGGAGAGCCATCCTTGGACACAGAGTGAGCAGGAGATGCGAATACGCTGTGGGAATCGGAGCCA TGTTCCTTGGCTTCTGGGTGCCGCTGGCTCCACCATGGGCGCTCCCATCACACTGACAGTGCAAGCCTATGA CCCTAGCAAAGACCTCATTGCTGAGATTCAGAAACAGGGTCAGGATCAGTGGACATATCAGATTTTCCAAGAGCCT GCACCCTCAACTTTCCCATTAGCAAAGGCAGCCCTGCTATCTTTCAGTCCAGCATGACACAGATTCTGGAGCCTTT TAGGAAACAAAACCCTGACATGGTCATCTATCAGTATCCTAGCCCTCTGACATTCGGATGGTGTTTCAAACTGGTC  ${\tt CCCGTGGACCCCAGCGAAGTGGAAGAGACCAACAAGGGCGAAAACAATTGCCTCCTGTTTAGGAAATACACAGCCT}$ TTACCATTCCCTCCACCAATAACGAAACCCCTGGCATTAGGTATCAGTATAACGTCCTGCCTCAGGGATGGGGAAG CACAATGGGAGCCGCCAGCATGACCCTCACCGTCCAGGCTAGGCAACTGCTCCAGCGAATCGTCCAGCAACAGAAC AATCTGCTGGAGGAGAATAGGGAAATCCTCAAAGAGCCTGTGCATGGCGTCTACTACGATCCCTCCAAGGATCTGA TCGCTGAAATCCAAAAGCAAGGCACAGAGGAACTGTCCGCCTTGGTGGATATGGGAAACTACCACCTCGGAGTGGA ATTGGCATCATCCGTCAGAGAAGGGCCCAGAGCTCCCAGGAAAAAGGGATGCTGGAAGTGTGGCAAAGAGGGACACC AGATGAAGGATTGCACTGAGAGACAGGCTAACTTTCTGGGAAAGGATGCCAGACTGGTTATCAAAACCTATTGGGG ACTGCATACCGGTGAGAGAGACTGGCACCTCGGCCATGGCGTCAGCATTGAGTGGAGGACAAGGGGAAAGGGCTGAG GATAGCGGCAACGAAAGCGAAGGCGACAGAGAAGAGCTCAGCACAATGGTGGACATGGGCAATTACGATCTGTCTA CAGGCTCGTGAATGGCAGTGAGGGCGAGGAAGTCAATAAGGGAGAATAACTGTCTGCTCCACCCTATGAGTCAA CATGGCATGGAAGACGAAGACAGAGGGTCAATAGCGATATCAAAGTGGTCCCCAGAAGGAAAGCCAAAATCATTA GGGATTACGGAAAGCAAATGGCTGACGATGACTGTGTGGCCGGCTTCTTCTCCGAGCAAACAAGGGCTAACTCCCC GAGGGACACATTGCCAAAAGCTGTAGGGCCCCTCGCAAGAAAGGTTGTTGGAAATGCGGAAGGGAAGGCCATCAAA TGAAAGACTGTACCGAAAGGCAAGCCAATTTCCTCGGCAAAATCTGGCCCTCCAAAAAAGGCAGACCCGGAAACTT TCTCCAAAGCAAATGGCTCTGGTATATCAAAATCTTTATCATGATCGTCGGTGGACTGATTGGCCTCAGGATTATC TTTGCCGTCCTGTCCATCATTAACGGGGCCGTGAGCCGAGACCTCGATAAACATGGCGCTATTACAAGCTCCAATA CCGCTGCCAATAACCCTGACTGTCTCGGCTGGAGGCTGCCCATGACACCCCTGGAGATCATCGCTATCGTCGC  ${\tt CCTTATCGTCGCCCTCATCATAGCCATTGTGGTCTGGACAATCGTCTACATTGAGTATGTCGACtgaagatctgaa}$ ttc

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### B1 fragment

ggatccaccATGCTCGAGAATATGCTCACCCAAATCGGATGCACACTGAATTTCCCTATCTCCCCCATTGAGACAG TGCCTGTGAAACTGAAACCCGGAATGGATGGCGCCGCCACCTTTAGGCCTGGCGGAGGCAATATCAAAGACAATTG GAGAAGCGAACTGTATAAGTATAAGGTCGTGAAGATTAAGCCTCTGGGAATCACATGGATTCCCGAATGGGAGTTC GTCAACACCCCCCACTGGTCAAGCTATGGTATCAGCTGGAGAAAGACCCTATCGTTGGCGTTGAGCCTCAGGATC CTCTGTCCTGTTTCTGGATGGCATTGACAAAGCTCAAGAGGAACATGAAAAGTATCACTCCAACTGGAGGACAATG GCCAACGACTTTAATCTGATGAAGCATCTCGTCTGGGCCTCTAGGGAGCTGGAGAGATTCGCTCTGAATCCCAGCC TGTCAAAACCATTATCGTCCAACTCAACGAAAGCGTCGAGATTAACATGGGCGCTAGGGCTAGTGTCCTCAGAGGC GCCTGGAGGGACTGGTTTACTCCAAAAAGAGGCAAGACATTCTGGATCTGTGGGTGTATAACACACAGGGATTCAC TAGATGGGGAACCATGATCCTCGGCTTGGTGATTATCTGTAGCGCCAGCGAGAATCTGTGGGTGACAGTGTATTAC GGAGTGCCTGTGTGGAGGAGACAGCTCCTGTCCGGCATTGTGCAACAACAAAATAACCTCCTGAGGGCTATCGAAG CCCAACAGCATCTGCTCCAGCTCACCGTCTGGGTCAGGCATTTCCCCAGGCCTTGGCTCCACGGCCTGGGACAGTA CATCTATGAGACATACGGAGACACATGGGCGGGAGTGGAAGCCCTCACAGCCCTCATCACACCCAAAAAGATTAGG CCTCCCCTCCCATCCGTGAAAAAGCTCACCGAAGACAGATGGAATGAGCCTCAAAAGACATATAGCGCTGGCGAAA GGATTATCGATATCATTGCATCCGACATTCAGACTAAGGAACTGCAAAAGCAAATCCTAAAGATTCAGAATTTCGC GCCACCGATATCATTCCCGTGGGCGAAATCTATAAGAGATGGATCATTCTGGGACTCAACAAAATCGTGAGAATGT ATCTACCCGTCAGCATTCTGGATATCAGAGTGAGACAGGGATACTCCCCCCTCAGCTTTCAGACACTGCTGCCCGC CCTCTGCCTCAGACAAGGGGAGACAATCCCACAGACCCTAAGGAAAAGGCAAAAAGGCTAGTGGAGGGGTCGAGTCCA TGAATAAGGAACTGAAAAAGATTATCGGACAGGTCAGGGACCAGGCTGAGCACCTGAAAACCGCTGTGCAAATGGC TGCCATGCAGATGCTCAAGGATACCATTAACGAAGAGGCTGCCGAGTGGGACAGAGTCCATCCCGTCCATGCCGGG CCCGTTCCCCCTCTCACCGAGATTTGTAAAGAAATGGAAAAAGGCCAAAATCTCCAAGATTGGCCCTGAGAATC CCTATAACACACCCATCTTTGCCATTCAAGTGAGAGAGCCAAGCCGAACACCTCAAGACAGCCGTCCAGATGGCAGT GACTTTAGGGAGCTCAACAAACGTACACAGGATTTCTGGGAGGTCCAGCTCGGCTTTTTGGCTCTGGGTTGGGATG ACCTCAGGAGCCTGTCTCTCAGCTATCACAGACTGAGAGACTTTATCCTCATCGTTGCCAGAATCTGCCGACA TAGCAGAATCGGCATCACTAGGCAACGTAGAGGTAGGAACGGCGCCCTCCAGTTCCGCTGCCCCCAAAATCTCCTTC GACCCCATTCCCATTCACTATTGCGCTCCCGCTGGCTTCGCTATCCTCAAGTGTAACGATAAGAACTTCAATGGCG CCTCGCCGATCAGCCTAGCCTCATCCCCTTAGCTTCCCTGAAAAGCCTCTTCGGAAACGATCCCTTATCCCAA GCCGCTAGAAGGGCTATCCTCGGCCATATAGTCAGGAGAGGTGTGAGTATCAGTCCGGACACAATAAGGTCGGCT CCCTGCAATACCTCGCACTCAGTCAACCCACAACCGCTTGCTACAAGTGTTACTGTAAGAAATGTTGCTTCCACTG AGCAGGCAAGACGAAGACGCAAGCAAGTACCATAGCAATTGGAGAACCATTGGCAATGAGTTTAACCTCCCCCTA TCGTCCCTAAGGAAATCGTCGCAAATTGCAATAAGTGTAACGAATGGACACTGGAACTGCTGGAGGAACTGAAACA TGAAGCCGTGAGACACTTTCCCAGACCCTGGCTGCATGGCCTCGGTCAACACGATATCATTAGCCTCTGGGATCAG

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TCCCTGAAACCCTGTGTGAAACTGACACCCCTCTGCGTCACCCTCAACTGTACCAATGCCAATCTGATGAAGAGAT ACTCCACCCAAGTGGACCCCGATCTGGCTGACCAACTGATTCACCTCCACTATTTCGATTGCCTTTTGCCGATAGCGC AATCCATCCCATCGGCCAACACGGAATGGAGGATGAGGGATGGGAAGTGCTGAAATGGAAATTCGATAGCCATCTG TGAAACACTGGCCCCTCACCGAAGAGAAAATCAAAGCCATTTGGCCTAGCAACAAGGGAAGGCCTGGCAATTTCCC GCAGTCCAGGCCTGAGCCTACCGCACCCCCAGCCGAGAGCTTTAGATTCGGCATTAGCAAAAAGGCTAAGGGATGG TTTTACAGACACCATTACGATAGCCGACACCCTAAGGTCAGCTCCGAGGTCCACATTCCCCTCGGCATGATGACCG CTTGCCAAGGCGTCGGCGGACCCAGTCACAAAGCCAGGGTACTGGCAGAGGCTATATCCCAGGTGAACAACGCTAA CATTCCTCCCATTGTGGCCAAAGAGATTGTGGCAAACTGTGACAAATGCCAGCTCAAGAGTGAGGCTATTCACGGA CAGGTGAACTGTAGCCCTTCCGAGGGAACAAGACAGACTAGGAAGAACAGACGTAGAAGGTGGCGTGCGAGGCAAA GGCAAATCCACTCCATCTCCGAGAGGATTCTGGGACAGATGAGGGAACCCAGAGGCTCCGACATTGCCGGTACTAC AAGCACACTGCAAGAGCAAATCGCATGGATGACAAGCAATCCCCCTAGCATTCAACAAGAGTTTGGCATTCCCTAT AACCCTCAGTCCCAGGGCGTCGTGGAAAGCATGAACAAAGAGCTAAAGAAAATCATTGGCAGACAGGAGATCCTCG ATCTCTGGGTCTACCATACCCAAGGCTATTTCCCTGACTGGCAGAATTACACACCCGGACCCGGAGTCAGATACCC TAGCAGAGAAAGACAGAGACAGATTCATTCTATTAACGAATGGATTCTCAGCAACTGCCTCGGCAGATCCGCTGAG CCTGTGCCTCTGCAACTGTATAAGACACTGAGAGCCGAACAGGCTACCCAAGAGGTCAAGAATTGGATGACCGAGA CACTGCTCGTGCAAAACGCTAACCCTGACTGTGAGAGAGTGTATCTGGCTTGGGTCCCCGCTCATAAAGGCATTGG CGGAAACGAACAGGTGGACAAACTGGTCAGCGCTGGCATTAGGAAAACAGACCCTAACCCTCAGGAAATCCATCTG TGAAATGCAATAACAAAAGGTTCAACGGAACTGGACCCAGTAAGAATGTGTCCACCGTCCAGTGTACCCATGGCCT AGAGCTCAAGAATAGCGCTATCTCCCTGCTCAACGCTACCGCTATCGCTGTGGCTGGACCGATAGGGTTATC GAAGTGGTTCAGTCCCGGCATCCCAAAGTGTCCAGCGAAGTGCATATCCCTCTGGGAGACGCTAGGCTCATCATTA GGACATACTGGGGCCTCCACACAGGCGCTGCTATGGGCGGTAAATGGTCCAAGTGCTCCCTCGTCGGATGGCCCGC AGTGAGAGAGAGAATCAGACAGCCCCCTGCCGCTGAGGGAGTGCTCAAGACCGGCAAGTACTCTAGGAAGAGG GGTGCCCATACCAATGACGTCAAGCAACTGACAGAGGCTGTGCAAAAGATTGCCACAGAGTCTAGCTGGGAGGGTC TGAAATACTGGGGGAATCTGCTCCAGTACTGGGGCCAGGAACTGAAAATCTCCGCCGTCAGCCTCCTGAATGCCAC AGCCATTGAGCTGCCTGAGAAAGGAAAGCTCGACCGTCAACGATATCCAAAAGCTCGTGGGAAAGCTCAACTGGGCA TCCCAGATTTACCCCGGAAGAGCCATTGAGGCTCAGCAACACATGCTGCAACTGACAGTGTGGGGCATTAAGCAAC TGCAAGCCAGAGTGCTCGCCATTGAGAGATACCTCGCCCTCCAGGATAGCGGATTGGAAGTGAATATCGTCACCGA TAGCCAATACGCTCTAGGCATCATTCAGGCTCAGCCTGACAAAAGCGAAAGGGAAATCTCCAACTATACCAATCAG ATTTACAAGATCCTCACCGAATCTCAAAATCAACAGGATAGGAATGAGAAAGACCTCCTGGCTCCCACAAAGGCTA AGAGAAGGGTCGTGCAAAGGGAAAAGCGTGCCGTCGGCATTGCCCTATGTTTCTCGGATTCCTCGGCGCTGCCAA ACCCAAAATGATCGGAGGCATTGGAGGCTTTATCAAAGTCAGGCAGTATGACCAAATCCTTATCGAAATCTGTGGA AACAAGGCTATCTCCTACCATAGGCTCAGGGATTTCATTCTGATCGTCGCTAGGATTGTGGAACTGCTCGGCCGTA GCTCCCTGAAAGGCCTCCAGAGAGGCACACTGAATGCCTGGGTGAAAGTGATTGAGGAAAAGGGATTCAGTCCCGA AGTGATTCCCATGTTTTCCGCTCTGTCCGAGGGAGCCACACTCGAGtgaagatctgaattc

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### B2 fragment

ggatccaccATGCTCGAGAATATGCTCACCCAAATCGGATGCACACTGAATTTCCCTATCTCCCCCATTGACACAG TGCCTGTGAAACTGAAACCCGGAATGGATGGCGCCGCCATCTTTAGGCCTGGCGGAGGCAATATGAAAGACAATTG GAGAAGCGAACTGTATAAGTATAAGGTCGTGAAGATTAAGCCTCTGGGAATCACATGGATTCCCGAATGGGAGTTC GTCAACACCCCCACTGGTCAAGCTATGGTATCAGCTGGAGAAAGAGCCTATCGTTGGCGCTGAGCCTCAGGATC CGCTGTCCTGTTTCTGGATGGCATTAACAAAGCTCAAGAGGAACATGAGAAGTATCACTCCAACTGGAGGACAATG GCCAACGACTTTAATCTGATGAAGCATCTCGTCTGGGCCTCTAGGGAGCTGGAGAGATTCGCTCTGAATCCCGGCC TGTCAAAACCATTATCGTCCACCTCAACGAAAGCGTCGAGATTAACATGGGCGCTAGGGCAAGTGTCCTCAGCGGC GGCAAGCTGGACGCCTGGGAAAAGATTAGGCTCAGGCCTGGCGGCAAGAAAAAGTATAGGCTCAAGGAGAAGGGAG GCCTGGACGGACTGATTTACTCCCAAAAGAGGCAAGACATTCTGGATCTGTGGGTGTATAACACACAGGGATTCAC TAGATGGGGAACCTTGATCCTCGGCTTGGTGATTATCTGTAGCGCCAGCGAGAATCTGTGGGTGACAGTGTATTAC GGAGTGCCTGTGGGAGAGACAGCTCCTGTCCGGCATTGTGCAACAGCAAAATAACCTCCTGAGGGCTATCGAAG CCCAACAGCATCTGCTCCAGCTCACCGTCTGGGTCAGGCATTTCCCCCAGGCCTTGGCTCCACAGCCTGGGACAGTA CATCTATGAGACATACGGAGACACATGGTCGGGAGTGGAAGCCCTCAAAGCCCTCATCAAACCCAAAAAGATTAAG CCTCCCTCCCATCCGTGAAAAAGCTCACCGAAGACAAATGGAATAAGCCTCAAAAGACATATAGCGCTGGCGAAA GGATTGTCGATATCATTGCAACCGACATTCAGACTAAGGAACTGCAAAACCAAATCATAAAGATTCAGAATTTCGC TGTGTTTATCCATAACTTTAAGAGGAAGGGAGGCATTGGCGGCTACTCCGCCGGAGAGAATCATTGACATTATC GCCAGCGATATCGTTCCCGTGGGCGATATCTATAAGAGATGGATCATTCTGGGACTCAACAAAATCGTGAGAATGT ATTCACCCGTCAGCATTCTGGATATCAGAGTGAGACAGGGATACTCCCCCCTCAGCTTTCAGACACTGATGCCCGC CCTCTGTCTCAGACAAGGGGAGACAATCCCACAGACCCTAAGGAAAAGGCAAAAAGGCTAGTGGAGTGGAGTCCA TGAATAAGGAACTGAAAAAGATTATCGGACAGGTCAGGGACCAGGCTGAGCACCTGAAAACCGCTGTGCAAATGGC CCTATAACACCCCGTCTTTGCCATTCAAGTGAGAGACCCAAGACACCCTCAAGACAGCCGTCCAGATGGCAGT GACTITAGGGAGCTCAACAAACGTACACAGGATTTCTGGGAGGTCCAGCTCGGCTTTTCGGCTCTGGCTTGGGATG ACCTCAGGAGCCTGTGTCTGTTCAGCTATCACAGACTGAGAGACTTTATCCTCATCGTTGCCAGAACCTGCCGACA TAGCAGAATCGCCATCACTAGGCAACGTAGAGGTAGGAACGCTCCTCCAGGTCCGCTGCCCCCAAAATCTCCTTC GACCCCATTCCCATTCACTATTGCGCTCCCGCTGGCTTCGCTATCCTCAAGTGTAACAATAAGACATTCAATGGCG CCTCGCCGATCAGCCTAGCCTCATCCTCCCTTAGCTTCCCTGAAAAGCCTCTTCGGAAACGATCCCTCATCCCAA GCCGCTAGAAGGGCTATCCTCGGCCAAATAGTCAGGAGAAGGTGTGAGTATCAGTCCGGACACAATAAGGTCGGCT CCCTGCAATACCTTGCACTCAGCCAACCCAAAACCGCTTGCTACAAGTGTTACTGTAAGAAATGTTGCTACCACTG TCAGGTCTGCTTCCTGAAGAAGGGACTGGGAATCAGGGATTACGGAAAGCAAATCGCTGGCCTGACTGTGTGGCC AGCAGGCAAGACGAAGACGCCAAGTACCATAGCAATTGGAGAACCATGGCCAGTGAGTTTAACCTCCCCCTA TCGTCGCTAAGGAAATCGTCGCAAGTTGTGATAAGTGTAACGAATGGACACTGGAACTGCTGGAAGCTGAAACA TGAAGCCGTGAGACACTTTCCCAGACCCTGGCTGCATGGCCTCGGTCAACACGATATCATTAGCCTCTGGGATCAG

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TCCCTGAAACCCTGTGTGAAACTGACACCCCTCTGCGTCACCCTCAACTGTACCAATGCCAATCTGCTGAAGAGCT ACTCCACCCAAGTGGACCCCGATCTGGCTGACCATCTGATTCACCTCCACTATTTCGATTGCTTTTCCGATAGCGC AATCCATCCCATGGGCCTACACGGAATGGAGGATGAGGGAAAGGGGAAGTGCTGAAAATGGAAATTCGATAGCCATCTG GCAGTCCAGGCCTGAGCCTACCGCACCCCCAGCCGAGAACTTTAGATTCGGCATTAGCAAAAAGGCTAAGGGATGG TTTTACAGACACCATTACGAAAGCCAACACCCTAAGGTCAGCTCCGAGGTCCACATTCCCCTCAGCATGATGACCG CTTGCCAAGGCGTCGGCGGACCCAGTCACAAAGCCAGGGTACTGGCAGAGGCTATGTCCCAGGTGAACAACGCTAA CATTCCTCCCATTGTGCCCAAAGAGATTGTGGCAAACTGTGACAAATGCCAGCTCAAGGGTGAGGCTATGCACGGA CAGGTGGACTGTAGCCCTTCCGAGGGATCAAGACAGGCTAGGAAGAACAGACGTAGAAGGTGGCGTGAGAGGCAAA GGCAAATCCGCGCCATCTCCGAGTGGATTCTGGGACAGATAAGGGAACCCAGAGGCTCCGACATTGCCGGTACCAC AAGCACACTGCAAGAGCAAATCGCATGGATGACAAACAATCCCCCTGGCATTAAGCAAGAGTTTGGCATTCCCTAT AACCCTCAGTCCCAGGGCGTCGTGGAAAGCATGAACAAAGAGCTCAAGAAAATCATTGGCAGACAGGAGATCCTCG ATCTCTGGGTCTACAATACCCAAGGCTTTTTCCCTGACTGGCAGAATTACACACCCGGACCCGGAATCAGATACCC TAGCAGAGCAAGACAGAGACAGATTCATGCTATTAGCGAAAGGATTCTCAGCAACTTCCTCGGCAGACCCGCTGAG CCTGTGCCTCTGCAACTGTATAAGACACTGAGAGCCGAACAGGCTACCCAAGAGGTCAAGAATTGGATGACCGACA CACTGCTCGTGCAAAACCCTGACTGTGAGAAAGTGTATCTGGCTTGGGTCCCCGCTCATAAAGGCATTGG CGGAAACGAACAGGTGGACAAACTGGTCAGCGCTTGGCATTAGGAAAACAGACCCTAACCCTCAGGAAATCGATCTG TGAAATGCAATAACAAAAAGTTCAACGGAACTGGACCCTGTAAGAATGTGTCCACCGTCCAGTGTACCCATGGCCT AGAGCTCAAGAATAGCGCTGTCTCCCTGCTCAACGCTACCGCTATCGCTGTGGCTGAGTGGACCGATAGGGTTATC GAAGTGGTTCAGTCCCAGCATCCCAAAGTGTCCAGCGAAGTGCATATCCCTCTGGGAGACGCTAGGCTCATTA AGACATACTGGGGCCTCCACACAGGCGCTGCTATGGGCGGTAAATGGTCCAAGTGCTCCCTCGTCGGATGGCCCGC AGTGAGAGAGAATCAGACAGACACCCCCTGCCGCTGAGGGAGTGCTCAAGACCGGCAAGTACTCCAGGATGAGG AGTGCCCATACCAATGACGTCAAGCAACTGACAGAGGTTGTGCAAAAGATTGCCACAGAGTCTAGCTGGGAGGGTC TGAAATACTTGTGGAATCTGCTCCTGTACTGGGGCCTGGAACTGAAAAACTCCGCCGTCAGCCTCCTGAATGCCAC AGCCATTGTGCTGCCTGAGAAAGAGGCTGGACCGTCAACGATATCCAAAAGCTCGTGGGAAAGCTCAACTGGGCA TCCCAGATTTACGCCGGAAGAGCCATTGAGGCTCAGCAACACTTGCTGCAACTGACAGTGTGGGGCATTAAGCAAC TGCAAGCCAGAGTGCTCGCCATTGAGAGATACCTCGCCCTCCAGGATAGCGGATCGGAAGTGAATATCGTCACCGA TAGCCAATACGCTCTAGGCATCATTCAGGCTCAGCCTGACAAAAGCGAAAGGGAAATCTCCAACTATACCAATCAG ATTTACAAGATCCTCACCGAATCTCAAAATCAACAGGATAGGAATGAGCAAGAACTCCTGGCTCCCACAAAGGCTA AGAGAAGGGTCGTGCAAAAGGGAAAAGCGTGCCGTCGGCATTGGCGCTATGTTTTTCGGATTCCTCGGCGCTGCCAA ACCCAAAATGATCGGAGGCATTGGAGGCTTTATCAAAGTCAGGCAGTATGACCAAATCCTTATCGAAATCTGTGGA CAGAAGGCTATCTCCTACCATAGGCTCAGGGATTTCATTCTGATCGTCGCTAGGATTGTGGAACTGCTCGGCCATA GCTCCCTGAGAGGCCTCCGGAGAGGCACACTGAATGCCTGGGTGAAAGTGGTTGAGGAAAAGGGATTCAATCCCGA AGTGATTCCCATGTTTACCGCTCTGTCCGAGGGAGCCACACTCGAGtgaagatctgaattc

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### C1 fragment

ggatccaccATGCTCGAGAGCAACACCCCGCTAATAATGCCGATTGCGCGTGGCTGAAAGCCCAGGAAGACGAAG AAGTGGGATTTCCTGTGAGACCCCAAGTGCCTAGAGCTTGGAGGGCTATCCTCAACATTCCCAGGAGGATTAGGCA AGGCTTTGAGAGAGCCCTCCTAGCCGCCGAATGGGACAGGGTTCACCCTGTGCACGCTGGCCCTGTCGCTCCCGGC CAAATGAGAGGCCCAGAGGAAGCGATATCGCTGGCACAACCCTCAGGCCCATGACATATAAGGCCGCTATTGACC TCAGCTTGTTTCTGAAAGAGAAAGGCGGACTGGAAGGCCTCATCTATAGCAAGAAAGCTGCTATGGAACAGGCTCC CAAGGCCAATGGACCTACCAAATCTTTCAGGAACCCTTTAAGAATCTGAAAACCGGAAAGTATTCCAGAATGAGAA GCGCTCACACAAACTGGATGACAGAAACCCTCCTGGTCCAGAATGCCAATCCCGATTGCAAGTCCATCCTCAGGGC TCTGGGAACCGGAGCCACACTGGAAGAGCCTGAGGTCATCCCTATGTTCTCAGCCCTCAGCGAAGGCGCTACCCCC CAAGACCTGAATACGATGCTCAACATCGTCAGCGGACACCAATCCACCCTCCAGGAACAGATTGGCTGGATGACAA ATAACCCTCCCATCCCTGTCGGAGAGATTTACAAAAGGTGGATTATCCTCGGCCTGACTAGAATCCCCCATCCCGC CGGCCTCAAGAAAAAGAAAAGCGTCACCGTCCTGGATGTGGGAGACGCTTACTTCAGCGTCCCCCTCGACGAAGAC CAAAAGGAAACCTGGGAGGCTTGGTGGACGGAATACTGGCAGGCTACCTGGATTCCTGAGTGGGAGTTTGTGAATA CCCCTCCCTCGTGTTTCCCGATTGGCATAACTATACCCCTGGCCCTGGCATAAGGTATCCCCTCACCTTTGGATG GTGCTTTAAGCTCGTGCCTGTGGACCCCAAACTGTGGTACCAACTGGAAAAGGAACCCATTGTCGGAGCCGAAACC TTTTACGTGGACGGAGCCGCCAACAGAGAGACAAAGCTCGGCCAAAACGTCCAGGGACAGATGGTGCATCAGGCTA TTAGCCCCAGGACCCTCAACGCTTGGGTCAAGGTCGTCGAAGAGAAAGCCTTTAACGAAACCGAAGTGCATAACGT CTGGGCTACCCATGCCTGTGCGTACCGATCCCCAATCCCCAAGAGATTCTCCTGGAGAATGTGACAGAGCTCAAG GATCAGAAACTCCTCGGCATTTGGGGATGCTCCGGCAAAATCATTTGCACAACCACTGTGCCTTGGAACAGCTCCT GGTCCAACCAAGCTGGCCATAACAAAGTGGGAAGCCTCCAGTATCTGGCTCTGACGGCTCTGATTAAGCCTAAGAA AATCAAACCCCCTCTGCCTAGCGTTAAGACAATCATTGTGCATCTGAATGAGTCCGTGGAAATCAATTGCACAAGG CCTAACAATAACACAAGGAAAGCCGCCGCTAGTGAAGTACGGAATAAGTCCAAACAGAAAACCCAGCAAGCTGCCG CCGATACAGGCGACTCCAGCCAGGTCAGCCAAAACTATCCCATTGTGTCAAACTTTACCTCCACCACTGTGAAAGC CGCTTGTTGGTGGGCCAATATCAAACAGGAGTTTGGAATCCCTTACAATCCCCAAAGCCAAACATTCTATGTGGAT GAATCTGGCAGCTCGACTGTACCCATCTGGAAGGCAAAGTCATTCTGGTAGCCGTCCACGTCGCCTCCGGCTACAT TGAGGCTGAGGTCGGCAATGAGCAAGTGGATAAGCTCGTGAGTTCCGGAATCAGAAAGGTGCTATTCCTCGACGGA ATCAATAAGGCTCAGGAAGAGCACGAAGTCAGGGAAAGGATTAGGCGAACCGCTCCCGCTGCTGAAGGCGTCGGCG CTGTCTCCCAGGATCTGGATAAGTACGGAGCCCTCACCTCCACAAGCGGAACCCAACAGTCCCAGGGAACTGAAAC TGGCGTCGGCAACCCTCAGATTTTGGGAGAGTCCAGCGTTGTCCTCGGCTCCGGCTCCATCGTCATCTGGGGTAAA ACCCCTAAGTTTAAGTTCCCCATTCAGAAAGAGACATGGGAAGCCTGGTGGACGGAGTATTGGCAAGCCGCTGCTT ACAGACTGATCAGCTGTAACACAGCGTTATCAAAACAGGCTTGCCCTAAGATTACCTTTGACCCTATCCCTATCCA GAAAAGGACTCCTGGACAGTGAATGACATTCAGAAATCAATTCTGAGAGCCCTCGGCCCAGGCGCTTCCCTGGAGG AAATGATGACAGCATGTCAGGGAGTGGGAGGCCCTGGCCATAAGGCTAGAGTGTATTACAGAGACTCCAGGGACCC CATTTGGAAAGGCCCTGCCAAACTGCTCTGGAAAGGCGAAGGCGCTGTGGTCATCCAAGACATTAAGATTGGAGGC CAACTGATAGAAGCCCTCCTGGATACAGGAGCCGATGACACCGTCCTGGAAGATATGAATCTGCCTGGCAAGTGGG GAATCAAACAGCTCCAGGCTAGGGTCCTGGCTATCGAGAGGTATCTGAAAGATCAACAGTTTCTGGGACTCTGGGG CTGTAGCGGAAAGGCTGCTATGGAAAACAGATGGCAAGTGATGATCGTCTGGCAAGTGGACAGGATGAAGATTAGG

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ACATGGAATAGCCTCGTGAAACACCATATGTATATTATCTGTACCACAACCGTCCCCTGGAACTCCACCTGGAGCA ATAAGTCCTTCGAAGAGATTTGGAATAACATGACCTGGATTCAATGGCTGATTCTCGCTATCGTCGTGTGGACCAT TGTGTATATCGAATACAAGAAACTGCTCAGGCAAAGGAGAATCGATAGGCTCATCAAAAGGCTCAACCCTGGCCTC CAATGAGTCCGAGGGAGACACCCCGGAATCAGATACCAATACAATGTGCTCCCCCAAGGCTGGAAGGGCTCCCCA CCCATTTTCCAAAGCTCCATGACCCAAATCCTCATGATGCAAAGGGAAACTTTAAGGGACAGAAAAGGATTATCA AGTGCTTCAACTGTGGAAAGGAAGGCCATCTCGCTAGGAATTGCAGACCTCCCCTAGAGAGACTGAACCTGGATTG  $\tt CTCCGAGGATAGCGACACCTCCGGCACACAGCAAAGCCAAGGCACAGAGACAGAAGTGGGACTCGTGGCTGTGCAT$ GTGGCCAGCGGATATATCGAAGCCGAAGTGATCCCTGCCGAAACTGGACAGGAAACCGCTTACTTTATCCTCAAGA TTAAGCCTGTGGTCAGCACACAGCTCCTGCTCAACGGTAGCCTCGCTGAAGAGGGAAATCATTATCAGAAGCGAAAA CTTTACCGATAACAAACTGGTCGGCAAACTGAATTGGGCTTCCCAAATCTACGCTGGCATCAAAGTGAAGCAACTG TGTAAGCTCCTGAGAGGCACCAAAGCCCTCACTCCTCTGTGTGACACTGAATTGCACAAACGCTAACCTCATCA CCCCTCTGGAAAGGCTCCACCTCGACTGTAGCGAAGACTGTGGCGAACTGGATAAGTGGGCCTCCCTGTGGAACT GGTTCAATATCACCAACTGGCTGTGGTACATTAAGATTTTCATTATGATTGTGGGAGGCAATAAGATTGTCAGGAT GTACTCACCTGTCTCCATCCTCGACATTAAGCAAGGCCCTAAGGAACCCTTCAGGGATTACGTGGACAGATTCGCT AAGCTCCTGTGGAAGGGAGGGGGGCCGTCGTGATTCAGGACAACTCCGACATTAAGGTCGTGCCCAGGAGAAAGG CTAAGATTATCGAACTGAATAAGAGAACCCAAGACTTTTGTGAAGTGCAACTGGGAATCCCTCACCCTGCTGGACT GAAGAAGAAAAGTCAGTGACAGTGGCCGCTATGAGAGTGAAAGAGACACAGATGAACTGGCCCAATCTGTGGAAG TGGGGCACAATGATTCTGGGACTGGTCATCATTTGCTCCGCCTCCATTAAGGTCAGACAGCTCTGCAAACTGCTCA GGGGTACAAAGGCTCTGACAGAGATTGTGACACTGACAGAGGAAGCCGGAACTGGAACTGCTCATATGGAAGTTTGA CTCCCGCCTCGCCCTGAGACATATCGCCAGGGAACTGCATCCCGAGTTCTACAAAGACTGCGCTGCTGTCGAGCTC CTGGGACGCTCCAGCCTCAAGGGACTGCAAAGGGGATGGGAAGGCCTCAAGTATTTGTGGAACCTCCTGCAGTATT GGGGCTCTAGCCTGGGGCAACTGCAACCTGCTCTGAAAACCGGATCAGAGGAACTGAAGTCCCTGTATAACACAAT CGCTACCCTCTGGTGTGTGCATCAGGAGCTCTACAAATACAAAGTGGTCAAAATCAAACCCCTCGGCATTGCCCCT ACCAGAGCCAAAAGGAGAGTGGTCGAGAGAGAGAAAAGGCTCACCGAAATCGTCCCACTCACCGAAGAGGCTGAGC TGGAGCTGGAGGAAAACAGAGAGATTCTGAGGGAACCCGTCCACGGAGTGTATAGAGTGCTCGCCGAAGCCATGAG CCAAGTCAACAATGCCAACATCATGATGCAGAGGGGCAATTTCAAAGGCCTAAAGAGAAATCATCAAACAAGAGGAA GAGGAGGTCGGCTTCCCCGTCAGGCCCCAGGTCCCACTGAGACCTATGACCTACAAAGGAGCCGTCGATCTGTCCT TCTTCAGACAGGGACCCAAAGAGCCTTTCAGAGACTATGTGGATAGGTTTTTCAAAACCCTCAGGGCTGAGCAAGC CTCACAGGAAGTGAAAAACTGGGAGAAAATCAGACTGAGACCTGGTGGCAAAAAGAAATACAAAATGAAACACATT GTGTGGGCCTCCAGGGAACTGGAAAGGTTTGCCTCCCAGTATGCCCTCGGCATCATCCTAGCCCAACCCGATAAGT CCGAGTCCGAGCTCGTGAATCAGATTATCGAAGAGCTCATCAAGAAGATTGCCGTCGCCGGATGGACAGAACA GGGCTGATGTGAAACAGCTCACCGCAGTCGTCCAGAAAATCGCTACCGAAAGCATTGTGATATGGGGAAAGACGCC CAAGTTCAGACTGCCTATCGCTGCCGCCAGCAACGAGAACATGGAGACCATGGCTGCTtgaagatctgaattc

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### C2 fragment

qqatccaccATGCTCGAGAGCAACACAGCCGCTAACAATACCGATTGCGTGTGGCTGAAAGCCCAGGAAGAGGAAG AAGTGGGATTTCCTGTGAGACCCCAAGTGCCTAGAGCCGGGGGGGCTATCCTCAACATTCCCACGAGGATTAGGCA AGGCCTTGAGAGAGCCCTCCTAGCCGCCGAATGGGATAGGATTCACCCTGTGCACGCTGGCCCTATCGCTCCCGGC CAAATGAGAGGCCCAGGGGAAGCGATATCGCTGGCACAACCCTCAGGCCCATGACATATAAGGCCGCTATTGACC TCAGCTTGTTTCTGAAAGAGAAAGGCGGACTGGATGGCCTCATCTATAGCAAGAAAGCTGCTATGGAACAGGCTCC CGAAGACCAAAGCTCTCAGAGAGAGCCTTACAATGAGTGGACCCTGGAGGCTCCTGGAAGAGCTCAAGCACGAGGCT CAAGGCCAATGGACCTTCCAAATCTTTCAGGAACCCTTTAAGAATCTGAAAACCGGAAAGTATGCCAGAATGAGAG GCGCTCACACAAACTGGATGACAGATACCCTCCTGGTCCAGAATGCCAATCCCGATTGCAAGTCCATCCTCAAGGC TCTGGGACCCGGAGCCTCACTGGAAGAGCCTGAGGTCATCCCTATGTTCTCAGCCCTCAGCGAAGGCGCTACCCCC CAAGACCTGAATATGATGCTCAACACCGTCGGCGGACACCAATCCACCCTCCAGGAACAGATTGGCTGGATGACAA ATAACCCTCCCATCCCTGTCGGAGAGATTTACAAAAGGTGGATTATCCTCGGCCTGACTAGAATCCCCCATCCCGC CGGCCTCAAGAAAAAGAAAAGCGTCACCGTCCTGGATGTGGGAGACGCTTACTTCAGCGTCCCCCTCGACGAAGGC CAAAGGGAAACCTGGGAGGCTTGGTGGATGGAATACTGGCAGGCTACCTGGATTCCTGAGGGGGAGTTTGTGAATA CCCCTCCCTCGTGTTTCCCGATTGGCAAAACTATACCCCTGGCCCTGGCACAAGGTATCCCCTCACCTTTGGATG GTGCTTTAAGCTCGTGCCTGTGGACCCCAAACTGTGGTACCAACTGGAAAAGGACCCCATTGTCGGAGTCGAAACC TTTTACGCGGACGGAGCCGCCAACAGAGAGACAAAGCTCGGCCAAAACGTCCAGGGACAGATGGTGCATCAGCCTA TTAGCCCCAGGACCCTCAACGCTTGGGTCAAGGTCATCGAAGAGAAAGGCTTTAGCGACACCGAAGTGCATAACGT CTGGGCTACCCATGCCTGTGTGCCTACCGATCCCCAATCCCCAAGAGATTCTCCTGGAGAATGTGACAGAGCTCAAG GATCAGAAACTCCTCGGCATTTGGGGATGCTCCGGCAAACTCATTTGCACAACCACTGTGCCTTGGAACAGCTCCT GGTCCAACCCAGCTGGCCATAACAAAGTGGGAAGCCTCCAGTATCTGGCTCTGAAGGCTCTGATTACGCCTAAGAA AATCAAACCCCCTCTGCCTAGCGTTAAGACAATCATTGTGCATCTGAATGAGTCCGTGGAAATCAATTGCACAAGG CCGATACAGGCAGCTCCAGCAAGGTCAGCCAAAACTATCCCATTGTGTCCCACCTTTACCTCCACCACTGTGAAAGC CGCTTGTTGGTGGGCCAATATCAAACAGGAGTTTGGAATCCCTTACAATCCCCAAAGCCGAACATTCTATGTGGAT GAATCTGGCAGCTCGACTGTACCCATCTGAAAGGCAAAGTCATTCTGGTAGCCGTCCACGTCGCCTCCGGCTACAT TGAGGCTGAGGTCGGCAATGAGCAAGTGGATAAGCTCGTGATTTCCGGGAATCAGAAAGGTGCTATTCCTCGACGGA ATCGATAAGGCTCAGGAAGGCACGAAGTCAGGGAAAGGATTAGGCGAGCCGCTCCCGCTGCTGAAGGCGTCGGCG CTGTCTCCCAGGATCTGGATAAGTACGGAGCCATCACCTCCACAAGCGGAACCCAACAGTCCCAGGGAACTGAAAC TGGCGTCGGCAACCCTCAGATTTTGGGAGAGTCCAGCGCTGTCCTCGGCTCCGGCTCCATCGTCATCTGGGGTAAA ACAGACTGATCAGCTGTAACACAAGCGTTATCACACAGGCTTGCCCTAAGATTAGCTTTGAGCCTATCCCTATCCA TTACTGTGCCCCTCCTAGCTGGATGGGCTATGAGCTCCACCCTGACAGATGGACAGTGCAACCCATCGTGCTCCCC GAAAAGGAGTCCTGGACAGTGAATGACATTCAGAAAACAATTCTGAAAGCCCTCGGCCCAGGCGCTACCCTGGAGG AAAATATGACAGCATGTCAGGGAGTGGGAGGCCCTGGCCATAAGGCTAGAGTGTATTACAGAGACTCCAGGGACCC CATTTGGAAAGGCCCTGCCAAACTGCTCTGGAAAGGCGAAGGCGCTGTGGTCATCCAAGACATTAAGATTGGAGGC CAACTGAAAGAAGCCCTCCTGGATACAGGAGCCGATGACACCGTCCTGGAAGATATCAATCTGCCTGGCAAGTGGG GAATCAAACAGCTCCAGGCTAGGGTCCTGGCTATCGAGAGGTATCTGAAAGATCAACAGCTTCTGGGAATCTGGAG CTGTAGCGGAAAGGCTGCTATGGAAAACAGATGGCAAGTGATGATCGTCTGGCAAGTGGACAGGATGAAGATTAGG

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ACATGGAATAGCCTCGTGAAACACCATATGTATCTTATCTGTACCACGCCGTCCCCTGGAACTCCACCTGGAGCA ATAAGTCCTTCGAAGAGATTTGGAATAACATGACCTGGATTGAATGGCTGATTATCGCTATCGTCGTGGGACCAT TGTGTTTATCGAATACAAGAAACTGCTCAGGCAAAGGAAAATCGATAGGCTCATCGAAAGGCTCAACCCTGGCCTC CAATGAGTCCGAGGGAGACACCCCGGAATCAGATACCAATACAATGTGCTCCCCCAAGGCTGGAAGGGCTCCCCA GCCATTTTCCAAAGCTCCATGACCAAAATCCTCATGATGCAAAGGGGAAACTTTAAGGGACAGAAAAGGATTATCA AGTGCTTCAACTGTGGAAAGGAAGGCCATCTCGCTAGGAATTGCAGACCTCCCCTGGAGAGACTGAACCTGGATTG CTCCGAGGATAGCGACACCTCCGGCACACAGCAAAGCCAAGGCACAGAGACAGGAGTGGGACTCGTGGCTGTGCAT GTGGCCAGCGGATATATCGAAGCCGAAGTGATCCCTGCCGAAACTGGACAGGAAACCGCTTACTTTCTCCTCAAGA TTAAGCCTGTGGTCAGCACACAGCTCCTGCTCAACGGTAGCCTCGCTGAAGAGGGAAATCATTATCAGAAGCGAAAA CTTTACCAATAACAAACTGGTCGGCAAACTGAATTGGGCTTCCCAAATCTACCCTGGCATCAAAGTGAGGCAACTG AGAGACAGACCCTTTTGACGCCGCCCTTAGCTCCACCTTTCTGGGAAGGTCTGTCGAACCCGTCCCCCTCCAGCTC CCCCTCTGGAAAGGCTCCACCTCGACTGTAGCGAAGACAGTGACGAACTGGATAAGTGGGCCTCCCTGTGGAACT GGTTCAATATCACCAACTGGCTGTGGTACATTAAGATTTTCATTATGATTGTGGGGAGGCAATAAGATTGTCAGGAT GTACCAACCTGTCTCCATCCTCGACATTAAGCAAGGCCCTAAGGAACCCTTCAGGGATTACGTGGACAGATTCGCT  ${\tt AAGCTCCTGTGGAAGGGAGGGGAGCCGTCGTGATTCAGGACAACTCCGACATTAAGGTCGTGCCCAGGAGAAAGG}$ CTAAGATTATCGAACTGAATAAGAGAACCCAAGACTTTTGGGAAGCGCAACTGGGAATCCCTCACCATGCTGGACT GAAAAAGAAAAAGTCCGTGACAGTGGCCGCTATGAGAGTGAAAGAGACACAGATGAACTGGCCCAATCTGTGGAAG TGGGGCACAATGATTCTGGGACTGGTCATCATTTGCTCCGCCTCCATTAAGGTCAAACAGCTCTGCAAACTGCTCA GGGGTGCAAAGGCTCTGATAGACATTGTGCCACTGACAGAGGAAGCCGAACTGGAACTGCTCATATGGAAGTTTGA CTCCCACCTCGCCCTGAGACATATCGCCAGGGAACTGCATCCCGAGTACTACAAAGACTGCGCTGCTGTCGAGCTC  $\tt CTGGGACGCTCAAGGAACTGCGAAGGGGATGGGAAGCCCTCAAGTATTTGTGGAACCTCCTGCAGTATT$ GGGGCTCTAGCCTGGAGCAACTGCAATCTGCTCTGAAAACCGGATCAGAGGAACTGAGGTCCCTGTTTAACACAGT CGCTACCCTCTGGTGTGCATCAGGAGCTCTACAAATACAAAGTGGTCAAAATCGAACCCCTCGGCATTGCCCCT ACCAAAGCCAAAAGGAGAGTGGTCCAGAGAGAGAAAAGGCTCACCGATATCGTCACACTCACCGAAGAGGCTGAGC TGGAGCTGGAGGAAAACAGAGAGATTCTGAAGGAACCCGTCCACGGAGTGTATAGAGTGCTCGCCGAAGCCATGAG CCAAGCCAACAATGCCAACATCATGATGCAGAGAGGGCAATTTCAGAGGGCCCAAAGAGAATCATCAAACAAGAGAAA GAGGGGGTCGCCTCCCCGTCAGGCCTCAGGTCCCACTGAGACCTATGACCTACAAAGCAGCCATCGATCTGTCCT TCTTCAAACAGGGACCCAAAGAGCCTTTCAGAGACTATGTGGATAGGTTTTTCAAAACCCTCAGGGCTGAGCAAGC CTCACAGGAAGTGAAAAACTGGGAGAAAATCAGACTGAGATCTGGTGGCAAAAAGAAATACAAACTGAAACACATT GTGTGGGCCTCCAGGAAACGTTTGCCTCCCAGTATGCCCTCGGCATCATCCTAGCCCAACCCGATAAGT CATTGAGGTCGTCCAAAGGGCTTGGAGAGCCATTCTGAATATCCCCAGGAGAATCAGACTAGACTAGACTCGCCGGA GGGCTGATGTGAAACAGCTCACCGAAGTCGTTCAGAAAAATCGCTACCGAAAGCATTGTGATATGGGGAAAGACACC CAAGTTCAGACAGCCTATCGCTGCCGCCAGCAACGAGAACATGGACGCCATGGCTGCTtqaaqatctqaattc

# INTERNATIONAL SEARCH REPORT

International application No.

		PCI//	AUU1/UU622		
A.	CLASSIFICATION OF SUBJECT MATTER				
Int. Cl. 7:	C07K 19/00; C12Q 1/68; C07K 2/00, 14/005, 14/15, 14/20, 14/435; C12N 15/09				
According to	International Patent Classification (IPC) or to both	national classification and IPC			
B.	FIELDS SEARCHED				
Minimum docu	umentation searched (classification system followed by	classification symbols)			
SEE ELECI	TRONIC DATABASES BELOW	· .			
	searched other than minimum documentation to the ex	tent that such documents are included in the	he fields searched		
	TORNIC DATABASES BELOW				
L	base consulted during the international search (name of MEDLINE: Combinatorial protein/peptide/p				
	thetic protein/peptide polypeptide	orypepude, generality shuming, c	ionam swapping,		
C.	DOCUMENTS CONSIDERED TO BE RELEVAN	r			
Category*	Citation of document, with indication, where app	propriate, of the relevant passages	Relevant to claim No.		
х	WO 00/18906 A. MAXYGEN INC. 6/4/00	0	All		
x	WO 99/41402 A. MAXYGEN INC. 19/8/99 ,		All		
x	WO 99/41369 A. MAXYGEN INC. 19/8/99		All		
х	WO 99/41368 A. MAXYGEN INC. 19/8/99		All		
x	Ryu DDY and Nam D-H. Recent progress in biotechnological engineering. Biotechnol Prog. Jan-Feb 2000. 16: 2-16.		All		
х	Punnonen J. Molecular breeding of allergy vaccines and antiallergic All cytokines. Int Arch Allergy Immunol. March 2000. 121: 173-182				
x	Further documents are listed in the continuati	on of Box C X See patent fam	nily annex		
* "A" "E" "L"	") "	priority date and not in conflict with understand the principle or theory ur document of particular relevance; the be considered novel or cannot be con inventive step when the document is	the application but cited to aderlying the invention e claimed invention cannot asidered to involve an taken alone e claimed invention cannot e step when the document is		
-p-	*8	combination being obvious to a person	on skilled in the art		
Date of the act	ual completion of the international search	Date of mailing of the international search	ch report		
1/8/01		7 Augus	1 2001		
Name and mailing address of the ISA/AU		Authorized officer			
PO BOX 200,	NPATENT OFFICE WODEN ACT 2606, AUSTRALIA	Cillian Allan			
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# INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU01/00622

	PCT/AU01/00622			
C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
Х	Coward E. Shufflet: shuffling sequences while conserving the k-let counts. Bioinformatics. 1999. 15(12): 1058-59.	60-77		
Х	Crameri A et al. DNA shuffling of a family of genes from diverse species accelerates directed evolution. Nature. 1998. 391: 288-291.	1,3,4-14, 30- 33,47		
x	Giver L and Arnold H. Combinatorial protein design by in vitro recombination. Curr Opin Chem Biol. 1998. 2: 335-338	1,3,4-14, 30- 33, 47		
X	Zhao H et al. Molecular evolution by staggered extension process (StEP) in vitro recombination. Nature Biotech. 1998. 16: 258-61.			
x	Patten P et al. Applications of DNA shuffling to pharmaceuticals and vaccines. Curr Opin Biotech. 1997. 8: 724-33	1, 3, 4-14, 19-33, 47		
х	Fisch I et al. A strategy of exon shuffling for making large peptide reperoires displayed on filamentous bacteriophage. Proc Nat Acad Sci USA. 1996. 93: 7761-66	1, 2, 4-14, 30-33, 47		
x	Stemmer WPC. DNA shuffling by random fragmentation and reassembly: in vitro recombination for molecular evolution. Proc Nat Acad Sci USA. 1994. 91: 10747-751.	1-18, 30-33, 47		
X	Stemmer WPC. Rapid evolution of a protein in vitro by DNA shuffling. Nature. 1994. 370: 389-391.	1, 2, 4-14, 30-33		
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PCT/AU01/00622 International application No.

END OF ANNEX

# INTERNATIONAL SEARCH REPORT Information on patent family members

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

	Patent Family Member		atent Document Cited in Search Report
66/14732 UA	.A 69614\Q	00/06611 UA	.A 30681\00 OW
66/24792 UA		EP 1117777	
AU32891/ 99			
AU 32910/99			
Eb 1023315		A 2/99	WO 99/41402 A.
Eb 1023343		98\1982£ UA	
Eb 1024613		86/016SE UA	
Eb 1029845		Eb 1023315	
		Eb 1023343	
		ED 10\$4973	
AU 26741/99	A 83£14/99 OW		
46/24/9ZUA			
AU 32891/99			
Eb 1023315			
Eb 1023343			
Eb 1026845			